

REPEAT SEQUENCES OF THE CA125 GENE AND THEIR USE FOR DIAGNOSTIC AND THERAPEUTIC INTERVENTIONS

CROSS REFERENCE TO RELATED APPLICATIONS

5 This application claims the benefit of U.S. Provisional Application Serial No. 60/284,175 filed April 17, 2001 and U.S. Provisional Application Serial No. 60/299,380 filed June 19, 2001, which are incorporated by reference in their entirety.

BACKGROUND OF THE INVENTION

10 The present invention relates generally to the cloning, identification, and expression of multiple repeat sequences of the CA125 gene *in vitro* and, more specifically, to the use of recombinant CA125 with epitope binding sites for diagnostic and therapeutic purposes.

15 CA125 is an antigenic determinant located on the surface of ovarian carcinoma cells with essentially no expression in normal adult ovarian tissue. Elevated in the sera of patients with ovarian adenocarcinoma, CA125 has played a critical role for more than 15 years in the management of these patients relative to their response to therapy and also as an indicator of recurrent disease.

20 It is well established that CA125 is not uniquely expressed in ovarian carcinoma, but is also found in both normal secretory tissues and other carcinomas (i.e., pancreas, liver, colon) [Hardardottir H *et al.*, Distribution of CA125 in embryonic tissue and adult derivatives of the fetal periderm, *Am J Obstet. Gynecol.* 163;6(1):1925-1931 (1990); Zurawski VR *et al.*, Tissue distribution and characteristics of the CA125 antigen, *Cancer Rev.* 11-12:102-108 (1988); and O'Brien TJ *et al.*, CA125 antigen in human amniotic fluid and fetal membranes, *Am J Obstet Gynecol.* 155:50-55, (1986); Nap M *et al.*, Immunohistochemical characterization of 22
25 monoclonal antibodies against the CA125 antigen: 2nd report from the ISOBM TD-1 workshop, *Tumor Biology* 17:325-332 (1996)]. Notwithstanding, CA125 correlates directly with the disease status of affected patients (i.e., progression, regression, and no change), and has become the "gold standard" for monitoring patients with ovarian carcinoma [Bast RC *et al.*, A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian
30 cancer, *N Engl J Med.* 309:883-887 (1983); and Bon GC *et al.*, Serum tumor marker

immunoassays in gynecologic oncology: Establishment of reference values, *Am J Obstet Gynecol.* 174:107-114 (1996)]. CA125 is especially useful in post-menopausal patients where endometrial tissue has become atrophic and, as a result, is not a major source of normal circulating CA125.

5 During the mid 1980's, the inventor of the present invention and others developed M11, a monoclonal antibody to CA125. M11 binds to a dominant epitope on the repeat structure of the CA125 molecule [O'Brien TJ *et al.*, New monoclonal antibodies identify the glycoprotein carrying the CA125 epitope, *Am J Obstet Gynecol* 165:1857-64 (1991)]. More recently, the inventor and others developed a purification and stabilization scheme for CA125, which allows
10 for the accumulation of highly purified high molecular weight CA125 [O'Brien TJ *et al.*, More than 15 years of CA125: What is known about the antigen, its structure and its function, *Int J Biological Markers* 13(4):188-195 (1998)].

15 Considerable progress has been made over the years to further characterize the CA125 molecule, its structure and its function. The CA125 molecule is a high molecular weight glycoprotein with a predominance of O-linked sugar side chains. The native molecule exists as a very large complex (~2-5 million daltons). The complex appears to be composed of an epitope containing CA125 molecule and binding proteins which carry no CA125 epitopes. The CA125 molecule is heterogenous in both size and charge, most likely due to continuous deglycosylation of the side chains during its life-span in bodily fluids. The core CA125 subunit is in excess of
20 200,000 daltons, and retains the capacity to bind both OC125 and M11 class antibodies. While the glycoprotein has been described biochemically and metabolically by the inventor of the present invention and others, no one has yet cloned the CA125 gene, which would provide the basis for understanding its structure and its physiologic role in both normal and malignant tissues.

25 Despite the advances in detection and quantitation of serum tumor markers like CA125, the majority of ovarian cancer patients are still diagnosed at an advanced stage of the disease-- Stage III or IV. Further, the management of patients' responses to treatment and the detection of disease recurrence remain major problems. There, thus, remains a need to significantly improve and standardize current CA125 assay systems. Further, the development of an early indicator of risk of ovarian cancer will provide a useful tool for early diagnosis and improved prognosis.

SUMMARY OF THE INVENTION

The CA125 gene has been cloned and multiple repeat sequences as well as the carboxy terminus have been identified. CA125 requires a transcript of more than 35,000 bases and occupies approximately 150,000 bp on chromosome 19q 13.2. The CA125 molecule comprises three major domains: an extracellular amino terminal domain (Domain 1); a large multiple repeat domain (Domain 2); and a carboxy terminal domain (Domain 3) which includes a transmembrane anchor with a short cytoplasmic domain. The amino terminal domain is assembled by combining five genomic exons, four very short amino terminal sequences and one extraordinarily large exon. This domain is dominated by its capacity for O-glycosylation and its resultant richness in serine and threonine residues.

The extracellular repeat domain, which characterizes the CA125 molecule, also represents a major portion of the CA125 molecular structure. It is downstream from the amino terminal domain and presents itself in a much different manner to its extracellular matrix neighbors. These repeats are characterized by many features including a highly-conserved nature and a uniformity in exon structure. But most consistently, a cysteine enclosed sequence may form a cysteine loop. Domain 2 comprises 156 amino acid repeat units of the CA125 molecule. The repeat domain constitutes the largest proportion of the CA125 molecule. The repeat units also include the epitopes now well-described and classified for both the major class of CA125 antibodies of the OC125 group and the M11 group. More than 60 repeat units have been identified, sequenced, and contiguously placed in the CA125 domain structure. The repeat sequences demonstrated 70-85% homology to each other. The existence of the repeat sequences was confirmed by expression of the recombinant protein in *E. coli* where both OC125/M11 class antibodies were found to bind to sites on the CA125 repeat.

The CA125 molecule is anchored at its carboxy terminal through a transmembrane domain and a short cytoplasmic tail. The carboxy terminal also contains a proteolytic cleavage site approximately 50 amino acids upstream from the transmembrane domain, which allows for proteolytic cleavage and release of the CA125 molecule.

The identification and sequencing of multiple repeat domains of the CA125 antigen provides potentially new clinical and therapeutic applications for detecting, monitoring and treating patients with ovarian cancer and other carcinomas where CA125 is expressed. For

example, the ability to express repeat domains of CA125 with the appropriate epitopes would provide a much needed standard reagent for research and clinical applications. Current assays for CA125 utilize as standards either CA125 produced from cultured cell lines or from patient ascites fluid. Neither source is defined with regard to the quality or purity of the CA125 molecule. The present invention overcomes the disadvantages of current assays by providing multiple repeat domains of CA125 with epitope binding sites. At least one or more of any of the more than 60 repeats shown in Table 16 can be used as a "gold standard" for testing the presence of CA125. Furthermore, new and more specific assays may be developed utilizing recombinant products for antibody production.

Perhaps even more significantly, the multiple repeat domains of CA125 or other domains could also be used for the development of a potential vaccine for patients with ovarian cancer. In order to induce cellular and humoral immunity in humans to CA125, murine antibodies specific for CA125 were utilized in anticipation of patient production of anti-ideotypic antibodies, thus indirectly allowing the induction of an immune response to the CA125 molecule. With the availability of recombinant CA125, especially domains which encompass epitope binding sites for known murine antibodies, it will be feasible to more directly stimulate patients' immune systems to CA125 and, as a result, extend the life of ovarian carcinoma patients.

The recombinant CA125 of the present invention may also be used to develop therapeutic targets. Molecules like CA125, which are expressed on the surface of tumor cells, provide potential targets for immune stimulation, drug delivery, biological modifier delivery or any agent which can be specifically delivered to ultimately kill the tumor cells. Humanized or human antibodies to CA125 epitopes could be used to deliver all drug or toxic agents including radioactive agents to mediate direct killing of tumor cells. Natural ligands having a natural binding affinity for domains on the CA125 molecule could also be utilized to deliver therapeutic agents to tumor cells.

CA125 expression may further provide a survival or metastatic advantage to ovarian tumor cells. Antisense oligonucleotides derived from the CA125 repeat sequences could be used to down-regulate the expression of CA125. Further, antisense therapy could be used in association with a tumor cell delivery system of the type described above.

Recombinant domains of the CA125 molecule also have the potential to identify small molecules, which bind to individual domains of the CA125 molecule. These small molecules could also be used as delivery agents or as biological modifiers.

In one aspect of the present invention, a CA125 molecule is disclosed comprising: (a) an extracellular amino terminal domain, comprising 5 genomic exons, wherein exon 1 comprises amino acids #1-33 of SEQ ID NO: 299, exon 2 comprises amino acids #34-1593 of SEQ ID NO: 299, exon 3 comprises amino acids #1594-1605 of SEQ ID NO: 299, exon 4 comprises amino acids #1606-1617 of SEQ ID NO: 299, and exon 5 comprises amino acids #1618-1637 of SEQ ID NO: 299; (b) a multiple repeat domain, wherein each repeat unit comprises 5 genomic exons, wherein exon 1 comprises amino acids #1-42 in any of SEQ ID NOS: 164 through 194; exon 2 comprises amino acids #43-65 in any of SEQ ID NOS: 195 through 221; exon 3 comprises amino acids #66-123 in any of SEQ ID NOS: 222 through 249; exon 4 comprises amino acids #124-135 in any of SEQ ID NOS: 250 through 277; and exon 5 comprises amino acids #136-156 in any of SEQ ID NOS: 278 through 298; and (c) a carboxy terminal domain comprising a transmembrane anchor with a short cytoplasmic domain, and further comprising 9 genomic exons, wherein exon 1 comprises amino acids #1-11 of SEQ ID NO: 300; exon 2 comprises amino acids #12-33 of SEQ ID NO: 300; exon 3 comprises amino acids #34-82 of SEQ ID NO: 300; exon 4 comprises amino acids #83-133 of SEQ ID NO: 300; exon 5 comprises amino acids #134-156 of SEQ ID NO: 300; exon 6 comprises amino acids #157-212 of SEQ ID NO: 300; exon 7 comprises amino acids #213-225 of SEQ ID NO: 300; exon 8 comprises amino acids #226-253 of SEQ ID NO: 300; and exon 9 comprises amino acids #254-284 of SEQ ID NO: 300.

In another aspect of the present invention, the N-glycosylation sites of the amino terminal domain marked (x) in Figure 8B are encoded at positions #81, #271, #320, #624, #795, #834, #938, and #1,165 in SEQ ID NO: 299.

In another aspect of the present invention, the serine and threonine O-glycosylation pattern for the amino terminal domain is marked (o) in SEQ ID NO: 299 in Figure 8B.

In another aspect of the present invention, exon 2 in the repeat domain comprises at least 31 different copies; exon 2 comprises at least 27 different copies; exon 3 comprises at least 28 different copies; exon 4 comprises at least 28 different copies, and exon 5 comprises at least 21 different copies.

In another aspect of the present invention, the repeat domain comprises 156 amino acid repeat units which comprise epitope binding sites. The epitope binding sites are located in the C-enclosure at amino acids #59-79 (marked C-C) in SEQ ID NO: 150 in Figure 5.

In another aspect, the 156 amino acid repeat unit comprises O-glycosylation sites at positions #128, #129, #132, #133, #134, #135, #139, #145, #146, #148, #150, #151, and #156 in SEQ ID NO: 150 in Figure 5C. The 156 amino acid repeat unit further comprises N-glycosylation sites at positions #33 and #49 in SEQ ID NO: 150 in Figure 5C. The repeat unit also includes at least one conserved methionine (designated M) at position #24 in SEQ ID NO: 150 in Figure 5C.

In yet another aspect, the transmembrane domain of the carboxy terminal domain is located at positions #230-252 (underlined) in SEQ ID NO: 300 of Figure 9B. The cytoplasmic domain of the carboxy terminal domain comprises a highly basic sequence adjacent to the transmembrane at positions #256-260 in SEQ ID NO: 300 of Figure 9B, serine and threonine phosphorylation sites at positions #254, #255, and #276 in SEQ ID NO: 300 in Figure 9B, and tyrosine phosphorylation sites at positions #264, #273, and #274 in SEQ ID NO: 300 of Figure 9B.

In another aspect of the present invention, an isolated nucleic acid of the CA125 gene is disclosed, which comprises a nucleotide sequence selected from the group consisting of: (a) the nucleotide sequences set forth in SEQ ID NOS: 49, 67, 81, 83-145, 147, 150, and 152; (b) a nucleotide sequence having at least 70% sequence identity to any one of the sequences in (a); (c) a degenerate variant of any one of (a) to (b); and (d) a fragment of any one of (a) to (c).

In another aspect of the present invention, an isolated nucleic acid of the CA125 gene, comprising a sequence that encodes a polypeptide with the amino acid sequence selected from the group consisting of: (a) the amino acid sequences set forth in SEQ ID NOS: 11-47, 50-80, 82, 146, 148, 149, 151, and 153-158; (b) an amino acid sequence having at least 50% sequence identity to any one of the sequences in (a); (c) a conservative variant of any one of (a) to (b); and (d) a fragment of any one of (a) to (c).

In yet another aspect, a vector comprising the nucleic acid of the CA125 gene is disclosed. The vector may be a cloning vector, a shuttle vector, or an expression vector. A cultured cell comprising the vector is also disclosed.

In yet another aspect, a method of expressing CA125 antigen in a cell is disclosed, comprising the steps of: (a) providing at least one nucleic acid comprising a nucleotide sequence selected from the group consisting of: (i) the nucleotide sequences set forth in SEQ ID NOS: 49, 67, 81, 83-145,

147, 150, and 152; (ii) a nucleotide sequence having at least 70% sequence identity to any one of the sequences in (i); (iii) a degenerate variant of any one of (i) to (ii); and (iv) a fragment of any one of (i) to (iii); (b) providing cells comprising an mRNA encoding the CA125 antigen; and (c) introducing the nucleic acid into the cells, wherein the CA125 antigen is expressed in the cells.

5 In yet another aspect, a purified polypeptide of the CA125 gene, comprising an amino acid sequence selected from the group consisting of: (a) the amino acid sequences set forth in SEQ ID NOS: 11-48, 50, 68-80, 82, 146, 148, 149, 150, 151, and 153-158; (b) an amino acid sequence having at least 50% sequence identity to any one of the sequences in (a); (c) a conservative variant of any one of (a) to (b); and (d) a fragment of any one of (a) to (c).

10 In another aspect, a purified antibody that selectively binds to an epitope in the receptor-binding domain of CA125 protein, wherein the epitope is within the amino acid sequence selected from the group consisting of: (a) the amino acid sequences set forth in SEQ ID NOS: 11-48, 50, 68-80, 146, 151, and 153-158; (b) an amino acid sequence having at least 50% sequence identity to any one of the sequences in (a); (c) a conservative variant of any one of (a) to (b); and (d) a fragment of any one of (a) to (c).

15 A diagnostic for detecting and monitoring the presence of CA125 antigen is also disclosed, which comprises recombinant CA125 comprising at least one repeat unit of the CA125 repeat domain including epitope binding sites selected from the group consisting of amino acid sequences set forth in SEQ ID NOS: 11-48, 50, 68-80, 82, 146, 150, 151, 153-161, and 162 (amino acids #1,643-11,438).

20 A therapeutic vaccine to treat mammals with elevated CA125 antigen levels or at risk of developing a disease or disease recurrence associated with elevated CA125 antigen levels is also disclosed. The vaccine comprises recombinant CA125 repeat domains including epitope binding sites, wherein the repeat domains are selected from the group of amino acid sequences consisting of SEQ ID NOS: 11-48, 50, 68-80, 82, 146, 148, 149, 150, 151, 153-161, and 162 (amino acids #1,643-11,438), and amino acids #175-284 of SEQ ID NO: 300. Mammals include animals and humans.

25 In another aspect of the present invention, an antisense oligonucleotide is disclosed that inhibits the expression of CA 125 encoded by: (a) the nucleotide sequences set forth in SEQ ID NOS: 49, 67, 81, 83-145, 147, 150, and 152; (b) a nucleotide sequence having at least 70% sequence identity to any one of the sequences in (a); (c) a degenerate variant of any one of (a) to (b); and (d) a fragment of any one of (a) to (c).

The preceeding and further aspects of the present invention will be apparent to those of ordinary skill in the art from the following description of the presently preferred embodiments of the invention, such description being merely illustrative of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates the cyanogen bromide digested products of CA125 on Western blot probed with M11 and OC125 antibodies. Table 1 shows the amino acid sequence derived from the amino terminal end of the 40 kDa cyanogen bromide peptide along with internal sequences obtained after protease digestion of the 40 kDa fragment (SEQ ID NOS: 1-4). SEQ ID NO: 1 is the amino terminal sequence derived of the 40 kDa peptide and SEQ ID NOS: 2, 3, and 4 reflect internal amino acid sequences derived from peptides after protease digestion of the 40 kDa fragment. Table 1 further provides a translation of the EST (BE005912) with homologous sequences (SEQ ID NOS: 5 and 6) either boxed or underlined. Protease cleavage sites are indicated by arrows.

Figure 2A illustrates PCR amplification of products generated from primers utilizing the EST sequence referred to in Figure 1, the amino acid sequence obtained from the 40 kDa fragment and EST sequence AA# 640762. Lane 1-2: normal; 3: serous ovarian carcinoma; 4: serous ovarian carcinoma; 5: mucinous ovarian carcinoma; 6: β -tubulin control. The anticipated size band 400 b is present in lane 3 and less abundantly in lane 4.

Figure 2B illustrates the RT-PCR that was performed to determine the presence or absence of CA125 transcripts in primary culture cells of ovarian tumors. This expression was compared to tubulin expression as an internal control. Lanes 1, 3, 5, 7, and 9 represent the primary ovarian tumor cell lines. Lanes 2, 4, 6, and 8 represent peripheral blood mononuclear cell lines derived from the corresponding patients in lanes 1, 3, 5, and 7. Lane 10 represents fibroblasts from the patient tumor in lane 9. Lanes 11 and 12 are CaOV3 and a primary tumor specimen, respectively.

Figure 3 illustrates repeat sequences determined by sequencing cloned cDNA from the 400 b band in Figure 2B. Placing of repeat sequences in a contiguous fashion was accomplished by PCR amplification and sequencing of overlap areas between two repeat sequences. A sample of the complete repeat sequences is shown in SEQ ID NOS: 158, 159, 160, and 161, which was obtained in this manner and placed next to each other based on overlap sequences. The complete list of repeat sequences that was obtained is shown in Table 21 (SEQ ID NO: 162).

Figure 4 illustrates three Western immunoblot patterns: Panel A = probed with M11, Panel B = probed with OC125 and Panel C = probed with antibody ISOBM 9.2. Each panel represents *E. coli* extracts as follows: lane 1 = *E. coli* extract from bacteria with the plasmid PQE-30 only. Lane 2 = *E. coli* extract from bacteria with the plasmid PQE-30 which includes the CA125 repeat unit. Lane 3 = *E. coli* extract from bacteria with the plasmid PQE-30 which includes the TADG-14 protease unrelated to CA125. Panel D shows a Coomassie blue stain of a PAGE gel of *E. coli* extract derived from either PQE-30 alone or from bacteria infected with PQE-30 - CA125 repeat (recombinant CA125 repeat).

Figure 5 represents Western blots of the CA125 repeat sequence that were generated to determine the position of the M11 epitope within the recombinant CA125 repeat. The expressed protein was bound to Ni-NTA agarose beads. The protein was left undigested or digested with Asp-N or Lys-C. The protein remaining bound to the beads was loaded into lanes 1, 2, or 3 corresponding to undigested, Asp-N digested and Lys-C digested, respectively. The supernatants from the digestions were loaded in lanes 4, 5, and 6 corresponding to undigested, Asp-N digested and Lys-C digested, respectively. The blots were probed with either anti-His tag antibody (A) or M11 antibody (B). Panel C shows a typical repeat sequence corresponding to SEQ ID NO: 150 with each exon defined by arrows. All proteolytic aspartic acid and lysine sites are marked with overhead arrow or dashes. In the lower panel, the O-glycosylation sites in exons 4 and 5 are marked with O, the N-glycosylation sites are marked with X plus the amino acid number in the repeat (#12, 33, and 49) the conserved methionine is designated with M plus the amino acid number (M#24), and the cysteine enclosure which is also present in all repeats and encompasses 19 amino acids between the cysteines is marked with C-C (amino acids #59-79). The epitopes for M11 and OC125 are located in the latter part of the C-enclosure or downstream from the C-enclosure.

Figure 6 illustrates a Northern blot analysis of RNA derived from either normal ovary (N) or ovarian carcinoma (T) probed with a P³² cDNA repeat sequence of CA125. Total RNA samples (10µg) were size separated by electrophoresis on a formaldehyde 1.2% agarose gel. After blotting to Hybond N, the lanes were probed with P³² radiolabelled 400 bp repeat (see Figure 2). Lane 1 represents RNA from normal ovarian tissue, and lane 2 represents RNA from serous ovarian tumor tissue.

Figure 7A is a schematic diagram of a typical repeat unit for CA125 showing the N-glycosylation sites at the amino end and the totally conserved methionine (M). Also shown is the proposed cysteine enclosed loop with antibody binding sites for OC125 and M11. Also noted are the highly O-glycosylated residues at the carboxy end of the repeat.

Figure 7B represents the genomic structure and exon configuration of a 156 amino acid repeat sequence of CA125 (SEQ ID NO: 163), which comprises a standard repeat unit.

Figure 7C lists the individual known sequences for each exon, which have been determined as follows: Exon 1 – SEQ ID NOS: 164-194; Exon 2 – SEQ ID NOS: 195-221; Exon 3 – SEQ ID NOS: 222-249; Exon 4 – SEQ ID NOS: 250-277; and Exon 5 – SEQ ID NOS: 278-298.

Figure 8A shows the genomic structure of the amino terminal end of the CA125 gene. It also indicates the amino composition of each exon in the extracellular domain.

Figure 8B illustrates the amino acid composition of the amino terminal domain (SEQ ID NO: 299) with each potential O-glycosylation site marked with a superscript (o) and N-glycosylation sites marked with a superscript (x). T-TALK sequences are underlined.

Figure 9A illustrates the genomic exon structure of the carboxy-terminal domain of the CA125 gene. It includes a diagram showing the extracellular portion, the potential cleavage site, the transmembrane domain and the cytoplasmic tail.

Figure 9B illustrates the amino acid composition of the carboxy terminal domain (SEQ ID NO: 300) including the exon boundaries, O-glycosylation sites (o), and N-glycosylation sites (x). The proposed transmembrane domain is underlined.

Figure 10 illustrates the proposed structure of the CA125 molecule based on the open reading frame sequence described herein. As shown, the molecule is dominated by a major repeat domain in the extracellular space along with a highly glycosylated amino terminal repeat. The molecule is anchored by a transmembrane domain and also includes a cytoplasmic tail with potential for phosphorylation.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, conventional molecular biology, microbiology, and recombinant DNA techniques may be used that will be apparent to those skilled in the relevant art. Such techniques are explained fully in the literature (see, e.g., Maniatis, Fritsch & Sambrook, "Molecular Cloning: A Laboratory Manual (1982); "DNA Cloning: A Practical

Approach," Volumes I and II (D. N. Glover ed. 1985); "Oligonucleotide Synthesis" (M. J. Gait ed. 1984); "Nucleic Acid Hybridization" (B. D. Hames & S. J. Higgins eds. (1985)); "Transcription and Translation" (B. D. Hames & S. J. Higgins eds. (1984)); "Animal Cell Culture" (R. I. Freshney, ed. (1986)); "Immobilized Cells And Enzymes" (IRL Press, (1986)); and B. Perbal, "A Practical Guide To Molecular Cloning" (1984)).

Therefore, if appearing herein, the following terms shall have the definitions set out below.

A "vector" is a replicon, such as plasmid, phage or cosmid, to which another DNA segment may be attached so as to bring about the replication of the attached segment.

A "DNA molecule" refers to the polymeric form of deoxyribonucleotides (adenine, guanine, thymine, or cytosine) in either single stranded form, or a double-stranded helix. This term refers only to the primary and secondary structure of the molecule, and does not limit it to any particular tertiary forms. Thus, this term includes double-stranded DNA found, inter alia, in linear DNA molecules (e.g., restriction fragments), viruses, plasmids, and chromosomes.

As used herein, the term "gene" shall mean a region of DNA encoding a polypeptide chain.

"Messenger RNA" or "mRNA" shall mean an RNA molecule that encodes for one or more polypeptides.

"DNA polymerase" shall mean an enzyme which catalyzes the polymerization of deoxyribonucleotide triphosphates to make DNA chains using a DNA template.

"Reverse transcriptase" shall mean an enzyme which catalyzes the polymerization of deoxy- or ribonucleotide triphosphates to make DNA or RNA chains using an RNA or DNA template.

"Complementary DNA" or "cDNA" shall mean the DNA molecule synthesized by polymerization of deoxyribonucleotides by an enzyme with reverse transcriptase activity.

An "isolated nucleic acid" is a nucleic acid the structure of which is not identical to that of any naturally occurring nucleic acid or to that of any fragment of a naturally occurring genomic nucleic acid spanning more than three separate genes. The term therefore covers, for example, (a) a DNA which has the sequence of part of a naturally occurring genomic DNA molecule but is not flanked by both of the coding sequences that flank that part of the molecule in the genome of

the organism in which it naturally occurs; (b) a nucleic acid incorporated into a vector or into the genomic DNA of a prokaryote or eukaryote in a manner such that the resulting molecule is not identical to any naturally occurring vector or genomic DNA; (c) a separate molecule such as a cDNA, a genomic fragment, a fragment produced by polymerase chain reaction (PCR), or a restriction fragment; and (d) a recombinant nucleotide sequence that is part of a hybrid gene, i.e., a gene encoding a fusion protein.

"Oligonucleotide", as used herein in referring to the probes or primers of the present invention, is defined as a molecule comprised of two or more deoxy- or ribonucleotides, preferably more than ten. Its exact size will depend upon many factors which, in turn, depend upon the ultimate function and use of the oligonucleotide.

"DNA fragment" includes polynucleotides and/or oligonucleotides and refers to a plurality of joined nucleotide units formed from naturally-occurring bases and cyclofuranosyl groups joined by native phosphodiester bonds. This term effectively refers to naturally-occurring species or synthetic species formed from naturally-occurring subunits. "DNA fragment" also refers to purine and pyrimidine groups and moieties which function similarly but which have non naturally-occurring portions. Thus, DNA fragments may have altered sugar moieties or inter-sugar linkages. Exemplary among these are the phosphorothioate and other sulfur containing species. They may also contain altered base units or other modifications, provided that biological activity is retained. DNA fragments may also include species which include at least some modified base forms. Thus, purines and pyrimidines other than those normally found in nature may be so employed. Similarly, modifications on the cyclofuranose portions of the nucleotide subunits may also occur as long as biological function is not eliminated by such modifications.

"Primer" shall refer to an oligonucleotide, whether occurring naturally or produced synthetically, which is capable of acting as a point of initiation of synthesis when placed under conditions in which synthesis of a primer extension product, which is complementary to a nucleic acid strand, is induced, i.e., in the presence of nucleotides and an inducing agent such as a DNA polymerase and at a suitable temperature and pH. The primer may be either single-stranded or double-stranded and must be sufficiently long to prime the synthesis of the desired extension product in the presence of the inducing agent. The exact length of the primer will depend upon many factors, including temperature, the source of primer and the method used. For example, for

diagnostic applications, depending on the complexity of the target sequence, the oligonucleotide primer typically contains 10-25 or more nucleotides, although it may contain fewer nucleotides.

The primers herein are selected to be "substantially" complementary to different strands of a particular target DNA sequence. This means that the primers must be sufficiently
5 complementary to hybridize with their respective strands. Therefore, the primer sequence need not reflect the exact sequence of the template. For example, a non-complementary nucleotide fragment may be attached to the 5' end of the primer, with the remainder of the primer sequence being complementary to the strand. Alternatively, non-complementary bases or longer sequences can be interspersed into the primer, provided that the primer sequence has sufficient
10 complementarity with the sequence or hybridize therewith and thereby form the template for the synthesis of the extension product.

As used herein, the term "hybridization" refers generally to a technique wherein denatured RNA or DNA is combined with complementary nucleic acid sequence which is either free in solution or bound to a solid phase. As recognized by one skilled in the art, complete
15 complementarity between the two nucleic acid sequences is not a pre-requisite for hybridization to occur. The technique is ubiquitous in molecular genetics and its use centers around the identification of particular DNA or RNA sequences within complex mixtures of nucleic acids.

As used herein, "restriction endonucleases" and "restriction enzymes" shall refer to bacterial enzymes which cut double-stranded DNA at or near a specific nucleotide sequence.

20 "Purified polypeptide" refers to any peptide generated from CA125 either by proteolytic cleavage or chemical cleavage.

"Degenerate variant" refers to any amino acid variation in the repeat sequence, which fulfills the homology exon structure and conserved sequences and is recognized by the M11, OC125 and ISOBM series of antibodies.

25 "Fragment" refers to any part of the CA125 molecule identified in a purification scheme.

"Conservative variant antibody" shall mean any antibody that fulfills the criteria of M11, OC125 or any of the ISOBM antibody series.

MATERIALS AND METHODS

A. Tissue collection, RNA Isolation and cDNA Synthesis

Both normal and ovarian tumor tissues were utilized for cDNA preparation. Tissues were routinely collected and stored at -80°C according to a tissue collection protocol.

5 Total RNA isolation was performed according to the manufacturer's instructions using the TriZol Reagent purchased from GibcoBRL (Catalog #15596-018). In some instances, mRNA was isolated using oligo dT affinity chromatography. The amount of RNA recovered was quantitated by UV spectrophotometry. First strand complementary DNA (cDNA) was synthesized using 5.0 µg of RNA and random hexamer primers according to the manufacturer's
10 protocol utilizing a first strand synthesis kit obtained from Clontech (Catalog #K1402-1). The purity of the cDNA was evaluated by PCR using primers specific for the β -tubulin gene. These primers span an intron such that the PCR products generated from pure cDNA can be distinguished from cDNA contaminated with genomic DNA.

B. Identification and Ordering of CA125 Repeat Units

15 It has been demonstrated that the 2-5 million dalton CA125 glycoprotein (with repeat domains) can be chemically segmented into glycopeptide fragments using cyanogen bromide. As shown in Figure 1, several of these fragments, in particular the 40 kDa and 60 kDa fragments, still bind to the to the two classical antibody groups defined by OC 125 and M11.

20 To convert CA125 into a consistent glycopeptide, the CA125 parent molecule was processed by cyanogen bromide digestion. This cleavage process resulted in two main fractions on commassie blue staining following polyacrylamide gel electrophoresis. An approximately 60 kDa band and a more dominant 40 kDa band were identified as shown in Figure 1. When a Western blot of these bands was probed with either OC125 or M11 antibodies (both of which define the CA125 molecule), these bands bound both antibodies. The 40 kDa band was
25 significantly more prominent than the 60 kDa band. These data thus established the likelihood of these bands (most especially the 40 kDa band) as being an authentic cleavage peptide of the CA125 molecule, which retained the identifying characteristic of OC125 and M11 binding.

30 The 40 kDa and 60 kDa bands were excised from PVDF blots and submitted to amino terminal and internal peptide amino acid sequencing as described and practiced by Harvard Sequencing , (Harvard Microchemistry Facility and The Biological Laboratories, 16 Divinity

Avenue, Cambridge, Massachusetts 02138). Sequencing was successful only for the 40 kDa band where both amino terminal sequences and some internal sequences were obtained as shown in Table 1 at SEQ ID NOS: 1-4. The 40 kDa fragment of the CA125 protein was found to have homology to two translated EST sequences (GenBank Accession Nos. BE005912 and AA640762). Visual examination of these translated sequences revealed similar amino acid regions, indicating a possible repetitive domain. The nucleotide and amino acid sequences for EST Genbank Accession No. BE005912 (corresponding to SEQ ID NO: 5 and SEQ ID NO: 6, respectively) are illustrated in Table 1. Common sequences are boxed or underlined.

In an attempt to identify other individual members of this proposed repeat family, two oligonucleotide primers were synthesized based upon regions of homology in these EST sequences. Shown in Table 2A, the primer sequences correspond to SEQ ID NOS: 7 and 8 (sense primers) and SEQ ID NOS: 9 and 10 (antisense primers). Repeat sequences were amplified in accordance with the methods disclosed in the following references: Shigemasa K *et al.*, p21: A monitor of p53 dysfunction in ovarian neoplasia, *Int. J. Gynecol. Cancer* 7:296-303 (1997) and Shigemasa K *et al.*, p16 Overexpression: A potential early indicator of transformation in ovarian carcinoma, *J. Soc. Gynecol. Invest.* 4:95-102 (1997). Ovarian tumor cDNA obtained from a tumor cDNA bank was used.

Amplification was accomplished in a Thermal Cycler (Perkin-Elmer Cetus). The reaction mixture consisted of 1U Taq DNA Polymerase in storage buffer A (Promega), 1X Thermophilic DNA Polymerase 10X Mg free buffer (Promega), 300mM dNTPs, 2.5mM MgCl₂, and 0.25mM each of the sense and antisense primers for the target gene. A 20 µl reaction included 1 µl of cDNA synthesized from 50ng of mRNA from serous tumor mRNA as the template. PCR reactions required an initial denaturation step at 94°C/1.5 min. followed by 35 cycles of 94°C/0.5 min., 48°C/0.5 min., 72°C/0.5 min. with a final extension at 72°C/7 min. Three bands were initially identified (»400 bp, »800 bp, and »1200 bp) and isolated. After size analysis by agarose gel electrophoresis, these bands as well as any other products of interest were then ligated into a T-vector plasmid (Promega) and transformed into competent DH5α strain of *E. coli* cells. After growth on selective media, individual colonies were cultured overnight at 37°C, and plasmid DNA was extracted using the QIAprep Spin Miniprep kit (Qiagen). Positive clones were identified by restriction digests using *Apa* I and *Sac* I. Inserts were sequenced using an ABI

automatic sequencer, Model 377, T7 primers, and a Big Dye Terminator Cycle Sequencing Kit (Applied Biosystems).

Obtained sequences were analyzed using the Pileup program of the Wisconsin Genetic's Computer Group (GCG). Repeat units were ordered using primers designed against two highly conserved regions within the nucleotide sequence of these identified repeat units. Shown in Table 2B, the sense and antisense primers (5'-GTCTCTATGTCAATGGTTTCACCC-3' / 5'-TAGCTGCTCTCTGTCCAGTCC-3' SEQ ID NOS: 301 and 302, respectively) faced away from one another within any one repeat creating an overlap sequence, thus enabling amplification across the junction of any two repeat units. PCR reactions, cloning, sequencing, and analysis were performed as described above.

C. Identification and Assembly of the CA125 Amino Terminal Domain

In search of open reading frames containing sequences in addition to CA125 repeat units, database searches were performed using the BLAST program available at the National Center for Biotechnology Information (www.ncbi.nlm.nih.gov/). Using a repeat unit as the query sequence, cosmid AC008734 was identified as having multiple repeat sequences throughout the unordered (35) contiguous pieces of DNA, also known as contigs. One of these contigs, #32, was found to have exons 1 and 2 of a repeat region at its 3' end. Contig#32 was also found to contain a large open reading frame (ORF) upstream of the repeat sequence. PCR was again used to verify the existence of this ORF and confirm its connection to the repeat sequence. The specific primers recognized the 3' end of this ORF (5'-CAGCAGAGACCAGCACGAGTACTC-3')(SEQ ID NO: 51) and sequence within the repeat (5'-TCCACTGCCATGGCTGAGCT-3')(SEQ ID NO: 52). The remainder of the amino-terminal domain was assembled from this contig in a similar manner. With each PCR confirmation, a new primer (see Table 10A) was designed against the assembled sequence and used in combination with a primer designed against another upstream potential ORF (Set 1: 5'-CCAGCACAGCTCTTCCCAGGAC-3' / 5'-GGAATGGCTGAGCTGACGTCTG-3')(SEQ ID NO: 53 and SEQ ID NO: 54); Set 2: 5'-CTTCCCAGGACAACCTCAAGG-3' / 5'-GCAGGATGAGTGAGCCACGTG-3'(SEQ ID NO: 55 and SEQ ID NO: 56); Set 3: 5'-GTCAGATCTGGTGACCTCACTG-3' / 5'-GAGGCACTGGAAAGCCCAGAG-3')(SEQ ID NO: 57 and SEQ ID NO: 58). Potential adjoining sequence (contig #7 containing EST AU133673) was also identified using contig #32 sequence as query sequence in database searches. Confirmation

primers were designed and used in a typical manner (5'-CTGATGGCATTATGGAACACATCAC-3' / 5'-CCCAGAACGAGAGACCACTGAG-3')(SEQ ID NO: 59 and SEQ ID NO: 60).

In order to identify the 5' end of the CA125 sequence, 5' Rapid Amplification of cDNA Ends (FirstChoice™ RLM-RACE Kit, Ambion) was performed using tumor cDNA. The primary PCR reaction used a sense primer supplied by Ambion (5'-GCTGATGGCGATGAATGAACACTG-3') (SEQ ID NO: 61) and an anti-sense primer specific to confirmed contig #32 sequence (5'-CCCAGAACGAGAGACCACTGAG-3')(SEQ ID NO: 62). The secondary PCR was then performed using nested primers, sense from Ambion (5'-CGCGGATCCGAACACTGCGTTTGCTGGCTTTGATG-3') (SEQ ID NO: 63) and the anti-sense was specific to confirmed contig #7 sequence (5'-CCTCTGTGTGCTGCTTCATTGGG-3')(SEQ ID NO: 64). The RACE PCR product (a band of approximately 300 bp) was cloned and sequenced as previously described.

D. Identification and Assembly of the CA125 Carboxy Terminal Domain

Database searches using confirmed repeat units as query also identified a cDNA sequence (GenBank AK024365) containing other repeat units, but also a potential carboxy terminal sequence. The contiguous nature of this sequence with assembled CA125 was confirmed using PCR (5'-GGACAAGGTCACCACACTCTAC-3' / 5'-GCAGATCCTCCAGGTCTAGGTGTG-3'), (SEQ ID NO: 303 and SEQ ID NO: 304, respectively) as well as contig and EST analysis.

E. Expression of 6xHis-tagged CA125 repeat in *E. coli*

The open reading frame of a CA125 repeat shown in Table 11 was amplified by PCR with the sense primer (5'-ACCGGATCCATGGGCCACACAGAGCCTGGCCC-3') (SEQ ID NO: 65) the antisense primer (5'-TGTAAGCTTAGGCAGGGAGGATGGAGTCC-3') (SEQ ID NO: 66) PCR was performed in a reaction mixture consisting of ovarian tumor cDNA derived from 50 ng of mRNA, 5 pmol each of sense and antisense primers for the CA125 repeat, 0.2 mmol of dNTPs, and 0.625 U of Taq polymerase in 1x buffer in a final volume of 25 ml. This mixture was subjected to 1 minute of denaturation at 95°C followed by 30 cycles of PCR consisting of the following: denaturation for 30 seconds at 95°C, 30 seconds of annealing at 62°C, and 1 minute of extension at 72°C with an additional 7 minutes of extension on the last cycle. The product was electrophoresed through a 2% agarose gel for separation. The PCR product was purified and digested with the restriction enzymes *Bam* HI and *Hind* III. This digested PCR product was then ligated into the expression vector pQE-30, which had also been digested with *Bam* HI and *Hind* III. This clone

would allow for expression of recombinant 6xHis-tagged CA125 repeat. Transformed *E. coli* (JM109) were grown to an OD₆₀₀ of 1.5-2.0 at 37°C and then induced with IPTG (0.1 mM) for 4-6 hours at 25°C to produce recombinant protein. Whole *E. coli* lysate was electrophoresed through a 12% SDS polyacrylamide gel and Coomassie stained to detect highly expressed proteins.

5 F. Western Blot Analysis

Proteins were separated on a 12% SDS-PAGE gel and electroblotted at 100V for 40 minutes at 4°C to nitrocellulose membrane. Blots were blocked overnight in phosphate-buffered saline (PBS) pH 7.3 containing 5% non-fat milk. CA125 antibodies M11, OC125, or ISOBM 9.2 were incubated with the membrane at a dilution of 5µg/ml in 5% milk/PBS-T (PBS plus 0.1% TX-100) and incubated for 2 hours at room temperature. The blot was washed for 30 minutes with several changes of PBS and incubated with a 1:10,000 dilution of horseradish peroxidase (HRP) conjugated goat anti-mouse IgG antibody (Bio-Rad) for 1 hour at room temperature. Blots were washed for 30 minutes with several changes of PBS and incubated with a chemiluminescent substrate (ECL from Amersham Pharmacia Biotech) before a 10-second exposure to X-ray film for visualization.

Figure 4 illustrates three Western immunoblot patterns of the recombinant CA125 repeat purified from *E. coli* lysate (lane 2) compared to *E. coli* lysate with no recombinant protein (lane 1-negative control) and a recombinant protein TADG-14 which is unrelated to CA125 (lane 3). As shown, the M11 antibody, the OC125 antibody and the antibody ISOBM 9.2 (an OC125-like antibody) all recognized the CA125 recombinant repeat (lane 2), but did *not* recognize either the *E. coli* lysate (lane 1) or the unrelated TADG-14 recombinant (lane 3). These data confirm that the recombinant repeat encodes both independent epitopes for CA125, the OC125 epitope and the M11 epitope.

20 G. Northern Blot Analysis

Total RNA samples (approximately 10µg) were separated by electrophoresis through a 25 6.3% formaldehyde, 1.2% agarose gel in 0.02 M MOPS, 0.05 M sodium acetate (pH 7.0), and 0.001 M EDTA. The RNAs were then blotted to Hybond-N (Amersham) by capillary action in 20x SSPE and fixed to the membrane by baking for 2 hours at 80°C. A PCR product representing one 400 bp repeat of the CA125 molecule was radiolabelled using the Prime-a-Gene Labeling System available from Promega (cat. #U1100). The blot was probed and stripped

according to the ExpressHyb Hybridization Solution protocol available from Clontech (Catalog #8015-1).

RESULTS

5 In 1997, a system was described by a co-inventor of the present invention and others for purification of CA125 (primarily from patient ascites fluid), which when followed by cyanogen bromide digestion, resulted in peptide fragments of CA125 of 60 kDa and 40 kDa [O'Brien TJ *et al.*, More than 15 years of CA125: What is known about the antigen, its structure and its function, *Int J Biological Markers* 13(4)188-195 (1998)]. Both fragments were identifiable by commassie blue staining on polyacrylamide gels and by Western blot. Both fragments were shown to bind both
10 OC125 and M11 antibodies, indicating both major classes of epitopes were preserved in the released peptides (Figure 1).

Protein sequencing of the 40 kDa band yielded both amino terminal sequences and some internal sequences generated by protease digestion (Table 1 – SEQ ID NOS: 1-4). Insufficient yields of the 60 kDa band resulted in unreliable sequence information. Unfortunately, efforts to amplify
15 PCR products utilizing redundant primers designed to these sequences were not successful. In mid 2000, an EST (#BE005912) was entered into the GCG database, which contained homology to the 40 kDa band sequence as shown in Table 1 (SEQ ID NOS: 5 and 6). The translation of this EST indicated good homology to the amino terminal sequence of the 40 kDa repeat (e.g. PGSRKFKTTE) with only one amino acid difference (i.e. an asparagine is present instead of phenylalanine in the EST
20 sequence). Also, some of the internal sequences are partially conserved (e.g. SEQ ID NO: 2 and to a lesser extent, SEQ ID NO: 3 and SEQ ID NO: 4). More importantly, all the internal sequences are preceded by a basic amino acid (Table 1, indicated by arrows) appropriate for proteolysis by the trypsin used to create the internal peptides from the 40 kDa cyanogen bromide repeat. Utilizing the combined sequences, those obtained by amino acid sequencing and those identified in the EST
25 (#BE005912) and a second EST (#AA640762) identified in the database, sense primers were created as follows: 5'-GGA GAG GGT TCT GCA GGG TC-3' (SEQ ID NO: 7) representing amino acids ERVLQG and anti-sense primer, 5' GTG AAT GGT ATC AGG AGA GG-3' (SEQ ID NO: 9) representing PLLIPF. Using PCR, the presence of transcripts was confirmed representing these sequences in ovarian tumors and their absence in normal ovary and either very low levels or no
30 detectable levels in a mucinous tumor (Figure 2A). The existence of transcripts was further

confirmed in cDNA derived from multiple primary ovarian carcinoma cell lines and the absence of transcripts in matched lymphocyte cultures from the same patient (Figure 2B).

After cloning and sequencing of the amplified 400 base pair PCR products, a series of sequences were identified, which had high homology to each other but which were clearly distinct repeat entities (Figure 3) (SEQ ID NOS: 158 through 161).

Examples of each category of repeats were sequenced, and the results are shown in Tables 3, 4, and 5. The sequences represent amplification and sequence data of PCR products obtained using oligonucleotide primers derived from an EST (Genbank Accession No. BE005912). Table 3 illustrates the amino acid sequence for a 400 bp repeat in the CA125 molecule, which is identified as SEQ ID NO: 11 through SEQ ID NO: 21. Table 4 illustrates the amino acid sequence for a 800 bp repeat in the CA125 molecule, which corresponds to SEQ ID NO: 22 through SEQ ID NO: 35. Table 5 illustrates the amino acid sequence for a 1200 bp repeat in the CA125 molecule, which is identified as SEQ ID NO: 36 through SEQ ID NO: 46. Assembly of these repeat sequences (which showed 75-80% homology to each other as determined by GCG Software (GCG = Genetics Computer Group) using the Pileup application) utilizing PCR amplification and sequencing of overlapping sequences allowed for the construction of a 9 repeat structure. The amino acid sequence for the 9 repeat is shown in Table 6 as SEQ ID NO: 47. The individual C-enclosures are highlighted in the table.

Using the assembled repeat sequence in Table 6 to search genebank databases, a cDNA sequence referred to as Genbank Accession No. AK024365 (entered on 9/29/00) was discovered. Table 7 shows the amino acid sequence for AK024365, which corresponds to SEQ ID NO: 48. AK024365 was found to overlap with two repeats of the assembled repeat sequence shown in Table 6. Individual C-enclosures are highlighted in Table 7.

The cDNA for AK024365 allowed alignment of four additional repeats as well as a downstream carboxy terminus sequence of the CA125 gene. Table 8 illustrates the complete DNA sequence of 13 repeats contiguous with the carboxy terminus of the CA125 molecule, which corresponds to SEQ ID NO: 49. Table 9 illustrates the complete amino acid sequence of the 13 repeats and the carboxy terminus of the CA125 molecule, which corresponds to SEQ ID NO: 50. The carboxy terminus domain was further confirmed by the existence of two EST's (Genbank Accession Nos. AW150602 and AI923224) in the genebank database, both of which

confirmed the stop-codon indicated (TGA) as well as the poly A signal sequence (AATAA) and the poly A tail (see Table 9). The presence of these repeats has been confirmed in serous ovarian tumors and their absence in normal ovarian tissue and mucinous tumors as expected (see Figure 2A). Also, the transcripts for these repeats have been shown to be present in tumor cell lines
5 derived from ovarian tumors, but not in normal lymphocyte cell lines (Figure 2B). Moreover, Northern blot analysis of mRNA derived from normal or ovarian carcinoma and probed with a P³² labeled CA125 repeat sequence (as shown in Figure 6) confirmed the presence of an RNA transcript in excess of 20 kb in ovarian tumor extracts (see Figure 2B).

To date, 45 repeat sequences have been identified with high homology to each other. To
10 order these repeat units, overlapping sequences were amplified using a sense primer (5' GTC TCT ATG TCA ATG GTT TCA CCC-3') (SEQ ID NO: 305) from an upstream repeat and an antisense primer from a downstream repeat sequence (antisense 5' TAG CTG CTC TCT GTC CAG TCC-3') (SEQ ID NO: 306). Attempts have been made to place these repeats in a contiguous fashion as shown in Figure 3. There is some potential redundancy. Further, there is evidence from overlapping sequences that some repeats exist in more than one location in the sequence giving a total of more than 60 repeats in the CA125 molecule (see Table 21 SEQ ID NO: 162).

Final confirmation of the relationship of the putative CA125 repeat domain to the known CA125 molecule was achieved by expressing a recombinant repeat domain in *E. coli*. In Figure 4,
expression of a recombinant CA125 repeat domain is shown in lane 2 compared to the vector alone in lane 1, Panel D. A series of Western blots representing *E. coli* extracts of vector alone in lane 1; CA125 recombinant protein lane in 2 and recombinant TADG-14 (an unrelated recombinant
20 protease), lane 3, were probed with the CA125 antibodies M11, Panel A; OC125, Panel B; and ISOBM 9.2, Panel C. In all cases, CA125 antibodies recognized only the recombinant CA125 antigen (lane 2 of each panel).

To further characterize the epitope location of the CA125 antibodies, recombinant CA125
25 repeat was digested with the endoprotease Lys-C and separately with the protease Asp-N. In both cases, epitope recognition was destroyed. As shown in Figure 5, the initial cleavage site for ASP-N is at amino acid #76 (indicated by arrow in Figure 5C). This sequence (amino acids # 1-76), a 17 kDa band, was detected with anti-histidine antibodies (Figure 5A, Lane 3) and found to have no
30 capacity to bind CA125 antibodies (Figure 5B, Lane 3). The upper bands in Figures 5A and 5B represent the undigested remaining portion of the CA125 recombinant repeat. From these data, one

can reasonably conclude that epitopes are either located at the site of cleavage and are destroyed by Asp-N or are downstream from this site and also destroyed by cleavage. Likewise, cleavage with Lys-C would result in a peptide, which includes amino acids # 68-154 (Figure 5C) and again, no antibody binding was detected. In view of the foregoing, it seems likely that epitope binding resides in the cysteine loop region containing a possible disulfide bridge (amino acids # 59-79). Final confirmation of epitope sites are being examined by mutating individual amino acids.

To determine transcript size of the CA125 molecule, Northern blot analysis was performed on mRNA extracts from both normal and tumor tissues. In agreement with the notion that CA125 may be represented by an unusually large transcript due to its known mega dalton size in tumor sera, ascites fluid, and peritoneal fluid [Nustad K *et al.*, CA125 – epitopes and molecular size, *Int. J of Biolog. Markers*, 13(4)196-199 (1998)], a transcript was discovered which barely entered the gel from the holding well (Figure 6). CA125 mRNA was only present in the tumor RNA sample and while a precise designation of its true size remains difficult due to the lack of appropriate standards, its unusually large size would accommodate a protein core structure in excess of 11,000 amino acids.

Evidence demonstrates that the repeat domain of the CA125 molecule encompasses a minimum of 45 different 156 amino acid repeat units and possibly greater than 60 repeats, as individual repeats occur more than once in the sequence. This finding may well account for the extraordinary size of the observed transcript. The amino acid composition of the repeat units (Figure 7A, 7C, Table 21) indicates that the sequence is rich in serine, threonine, and proline typical of the high STP repeat regions of the mucin genes [Gum Jr., JR, Mucin genes and the proteins they encode: Structure, diversity and regulation, *Am J Respir. Cell Mol. Biol.* 7:557-564 (1992)]. Results suggest that the downstream end of the repeat is heavily glycosylated.

Also noteworthy is a totally conserved methionine at position 24 of the repeat (Figure 7A, 7C). It is this methionine which allowed cyanogen bromide digestion of the CA125 molecule, resulting in the 40 kDa glycopeptide that was identified with OC125 and M11 antibodies in Western blots of the CNBr digested peptides. These data predict that the epitopes for the CA125 antibodies are located in the repeat sequence. By production of a recombinant product representing the repeat sequence, results have confirmed this to be true. A potential disulfide bond is noted, which would encompass a C-enclosure comprising 19 amino acids enclosed by two cysteines at positions #59 and #79. The cysteines are totally conserved, which suggest a biological role for the resulting putative C-enclosure in each repeat. As mentioned above, it is likely that the OC125 and M11 epitopes are

located in the C-enclosure, indicating its relative availability for immune detection. This is probably due to the C-enclosure structure and the paucity of glycosylation in the immediate surrounding areas. Domain searches also suggest some homology in the repeat domain to an SEA domain commonly found in the mucin genes [Williams SJ *et al.*, MUC13, a novel human cell surface mucin expressed by epithelial and hemopoietic cells, *J of Biol. Chem* 276(21)18327-18336 (2001)] beginning at amino acid #1 and ending at #131 of each repeat. No biological function has been described for this domain.

Based on homology of the repeat sequences to chromosome 19q 13.2 (cosmid #AC008734) and confirmed by genomic amplification, it has been established that each repeat is comprised of 5 exons (covering approximately 1900 bases of genomic DNA): exon 1 comprises 42 amino acids (#1-42); exon 2 comprises 23 amino acids (#43-65); exon 3 comprises 58 amino acids (#66-123); exon 4 comprises 12 amino acids (#124-135); and exon 5 comprises 21 amino acids (#136-156) (see Figure 7B). Homology pile-ups of individual exons have also been completed (see Figure 7C), which indicates that exon 1 has a minimum of 31 different copies of the exon; exon 2 has 27 copies; exon 3 has 28 copies, exon 4 has 28 copies and exon 5 has 21 copies. If all exons were only found in a single configuration relative to each other, one could determine that a minimum number of repeats of 31 were present in the CA125 molecule. Using the exon 2 pile-up data as an example, it has been established as mentioned above that there are 27 individual exon 2 sequences. Using exon 2, which was sequenced fully in both the repeat units and the overlaps, results established that a minimum of 45 repeat units are present when exon 2 is combined with unique other exon combinations. However, based on overlap sequence information, 60+ repeat units are likely present in the CA125 molecule (Table 21). This larger number of repeat units can be accounted for by the presence of the same repeat unit occurring in more than one location.

Currently, the repetitive units of the repeat domain of the CA125 molecule constitute the majority of its extracellular molecular structure. These sequences have been presented in a tandem fashion based on overlap sequencing data. Some sequences may be incorrectly placed and some repeat units may not as yet be identified (Table 21). More recently, an additional repeat was identified in CA125 as shown in Tables 22 and 23 (SEQ. ID NOS: 307 and 308). The exact position has not yet been identified. Also, there is a potential that alternate splicing and/or mutation could account for some of the repeat variants that are listed. Studies are being conducted to compare both normal tissue derived CA125 repeats to individual tumor derived CA125 repeats to determine if such

variation is present. Currently, the known exon configurations would easily accommodate the greater than 60 repeat units as projected. It is, therefore, unlikely that alternate splicing is a major contributor to the repetitive sequences in CA125. It should also be noted that the genomic database for chromosome 19q 13.2 only includes about 10 repeat units, thus indicating a discrepancy between the data of the present invention (more than 60 repeats) and the genomic database. A recent evaluation of the methods used for selection and assembly for genomic sequence [Marshall E, DNA Sequencing: Genome teams adjust to shotgun marriage, *Science* 292:1982-1983 (2001)] reports that "more research is needed on repeat blocks of almost identical DNA sequence which are more common in the human genome. Existing assembly programs can't handle them well and often delete them." The CA125 repeat units located on chromosome 19 may well be victims of deletion in the genomic database, thus accounting for most CA125 repeat units absent from the current databases.

A. Sequence Confirmation and Assembly of the Amino Terminal Domain (Domain 1) of the CA125 Molecule

As previously mentioned, homology for repeat sequences was found in the chromosome 19 cosmid AC008734 of the GCG database. This cosmid at the time consisted of 35 unordered contigs. After searching the cosmid for repeat sequences, contig #32 was found to have exons 1 and 2 of a repeat unit at its 3' end. Contig #32 also had a large open reading frame upstream from the two repeat units, which suggested that this contig contained sequences consistent with the amino terminal end of the CA125 molecule. A sense primer was synthesized to the upstream non-repeat part of contig #32 coupled with a specific primer from within the repeat region (see Methods). PCR amplification of ovarian tumor cDNA confirmed the contiguous positioning of these two domains.

The PCR reaction yielded a band of approximately 980bp. The band was sequenced and found to connect the upstream open reading frame to the repeat region of CA125. From these data, more primer sets (see Methods) were synthesized and used in PCR reactions to piece together the entire open reading frame contained in contig #32. To find the 5' most end of the sequence, an EST (AU133673) was discovered, which linked contig #32 to contig #7 of the same cosmid. Specific primers were synthesized, (5'-CTGATGGCATTATGGAACACATCAC-3' (SEQ ID NO: 59) and 5'-CCCAGAACGAGAGACCAGTGAG-3' (SEQ ID NO: 60)), to the EST and contig #32. A PCR reaction was performed to confirm that part of the EST sequence was in fact contiguous with contig #32. Confirmation of this contiguous 5' prime sequencing strategy using overlapping sequences allowed the assembly of the 5' region (Domain 1) (Figure 8A). 5' RACE PCR was performed on

tumor cDNA to confirm the amino terminal sequence to CA125. The test confirmed the presence of contig #7 sequence at the amino terminal end of CA125.

The amino terminal domain comprises five genomic exons covering approximately 13,250 bp. Exon 1, a small exon, (amino acids #1-33) is derived from contig #7 (Figure 8A). The remaining
5 exons are all derived from contig #32: Exon 2 (amino acids #34-1593), an extraordinarily large exon, Exon 3 (amino acids #1594-1605), Exon 4 (amino acids #1606-1617) and Exon 5 (amino acids #1618-1637) (see Figure 8A).

Potential N-glycosylation sites marked (x) are encoded at positions #81, #271, #320, #624, #795, #834, #938, and #1,165 (see Figure 8B). O-glycosylation sites are extraordinarily abundant
10 and essentially cover the amino terminal domain (Figure 8B). As shown by the O-glycosylation pattern, Domain 1 is highly enriched in both threonine and serine (Figure 8B).

B. Sequence Confirmation and Assembly of the CA125 Carboxy Terminal End (Domain 3)

A search of Genbank using the repeat sequences described above uncovered a cDNA
15 sequence referred to as Genbank accession number AK024365. This sequence was found to have 2 repeat sequences, which overlapped 2 known repeat sequences of a series of 6 repeats. As a result, the cDNA allowed the alignment of all six carboxy terminal repeats along with a unique carboxy terminal sequence. The carboxy terminus was further confirmed by the existence of two other ESTs (Genbank accession numbers AW150602 and A1923224), both of which confirmed a stop codon as well as a poly-A signal sequence and a poly-A tail (see GCG database #AF414442). The sequence of
20 the carboxy terminal domain was confirmed using primers designed to sequence just downstream of the repeat domain (sense primer 5' GGA CAA GGT CAC CAC ACT CTA C-3') (SEQ ID NO: 303) and an antisense primer (5'-GCA GAT CCT CCA GGT CTA GGT GTG-3') (SEQ ID NO: 304) designed to carboxy terminus (Figure 9A).

The carboxy terminal domain covers more than 14,000 genomic bp. By ligation, this domain
25 comprises nine exons as shown in Figure 9A. The carboxy-terminus is defined by a 284 amino acid sequence downstream from the repeat domains (see Figure 9B). Both N-glycosylation sites marked (x) (#31, #64, #103, #140, #194, #200) and a small number of O-glycosylation sites marked (o) are predicted for the carboxy end of the molecule (Figures 9A, 9B). Of special note is a putative transmembrane domain at positions #230-#252 followed by a cytoplasmic domain, which is
30 characterized by a highly basic sequence adjacent to the membrane (#256-#260) as well as several

potential S/T phosphorylation sites (#254, #255, #276) and tyrosine phosphorylation sites (at # 264, #273, #274) (Figures 9A, 9B).

Assembly of the CA125 molecule as validated by PCR amplification of overlap sequence provides a picture of the whole molecule (see Figure 10 and Table 21). The complete nucleotide sequence is available in Genbank, Accession #AF414442 and the amino acid sequence as currently aligned is shown in Table 21.

DISCUSSION

The CA125 molecule comprises three major domains; an extracellular amino terminal domain (Domain 1), a large multiple repeat domain (Domain 2) and a carboxy terminal domain (Domain 3), which includes a transmembrane anchor with a short cytoplasmic domain (Figure 10). The amino terminal domain is assembled by combining five genomic exons, four very short amino terminal sequences and one extraordinarily large exon, which often typifies mucin extracellular glycosylated domains [Desseyn JL *et al.*, Human mucin gene MUC5B, the 10.7-kb large central exon encodes various alternate subdomains resulting in a super-repeat. Structural evidence for a 11p15.5 gene family, *J. Biol. Chem.* 272(6):3168-3178 (1997)]. This domain is dominated by its capacity for O-glycosylation and its resultant richness in serine and threonine residues. Overall, the potential for O-glycosylation essentially covers this domain and, as such, may allow the carbohydrate superstructure to influence ECM interaction at this end of the CA125 molecule (Figure 8). There is one short area (amino acids # 74-120) where little or no glycosylation is predicted, which could allow for protein-protein interaction in the extracellular matrix.

Efforts to purify CA125 over the years were obviously complicated by the presence of this amino terminal domain, which is unlikely to have any epitope sites recognized by the OC125 or M11 class antibodies. As the CA125 molecule is degraded *in vivo*, it is likely that this highly glycosylated amino terminal end will be found associated with varying numbers of repeat units. This could very well account for both the charge and size heterogeneity of the CA125 molecule so often identified from serum and ascites fluid. Also of note are two T-TALK sequences at amino acids # 45-58 (underlined in Figure 8B), which are unique to the CA125 molecule.

The extracellular repeat domain, which characterizes the CA125 molecule, also represents a major portion of the molecular structure. It is downstream from the amino terminal domain and presents itself in a much different manner to its extracellular matrix neighbors. These repeats are characterized by many features including a highly-conserved nature (Figure 3) and a uniformity in

exon structure (Figure 7). But most consistently, a cysteine enclosed sequence may form a cysteine loop (Table 21). This structure may provide extraordinary potential for interaction with neighboring matrix molecules. Domain 2 encompasses the 156 amino acid repeat units of the CA125 molecule. The repeat domain constitutes the largest proportion of the CA125 molecule (Table 21 and Figure 10). Because it has been known for more than 15 years that antibodies bind in a multivalent fashion to CA125, it has been predicted that the CA125 molecule would include multiple repeat domains capable of binding the OC125 and M11 class of sentinel antibodies which define this molecule [O'Brien *et al.*, New monoclonal antibodies identify the glycoprotein carrying the CA125 epitope, *Am J Obstet Gynecol.* 165:1857-1964 (1991); Nustad K *et al.*, Specificity and affinity of 26 monoclonal antibodies against the CA125 antigen: First report from the ISOBM TD-1 workshop, *Tumor Biology* 17:196-219 (1996); and Bast RC *et al.*, A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian cancer, *N. Engl. J. Med.* 309:883-887 (1983)]. In the present invention, more than 60 repeat units have been identified, which are in tandem array in the extracellular portion of the CA125 molecule. Individual repeat units have been confirmed by sequencing and further identified by PCR amplification of the overlapping repeat sequences. Results confirm the contiguous placement of most repeats relative to its neighbor (Table 21).

Initial evidence suggests that this area is a potential site for antibody binding and also for ligand binding. The highly conserved methionine and several highly conserved sequences within the repeat domain also suggests a functional capacity for these repeat units. The extensive glycosylation of exons 4 & 5 of the repeat unit and the N-glycosylation potential in exon 1 and the 5' end of exon 2 might further point to a functional capacity for the latter part of exon 2 and exon 3 which includes the C-enclosure (see Figure 7). It should be apparent that the C-enclosure might be a prime target for protease activity and such cleavage may well explain the difficulty experienced by many investigators in obtaining an undigested CA125 parent molecule. Such activity might explain the diffuse pattern of antibody binding and the loss of antibody binding for molecules of less than 200,000 kDa. Proteolysis would destroy the epitopes and, therefore, only multiple repeats could be identified by blotting with CA125 antibodies. The repeat unit organization also suggests the potential for a multivalent interaction with extracellular entities.

The carboxy terminal domain of the CA125 molecule comprises an extracellular domain, which does not have any homology to other known domains. It encodes a typical transmembrane domain and a short cytoplasmic tail. It also contains a proteolytic cleavage site approximately 50

amino acids upstream from the transmembrane domain. This would allow for proteolytic cleavage and release of the CA125 molecule (Figure 9). As indicated by Fendrick, *et al.* [CA125 phosphorylation is associated with its secretion from the WISH human amnion cell line, *Tumor Biology* 18:278-289 (1997)], release of the CA125 molecule is preceded by phosphorylation and sustained by inhibitors of phosphatases, especially inhibition of phosphatase 2B. The cytoplasmic tail which contains S/T phosphorylation sites next to the transmembrane domain and tyrosine phosphorylation sites downstream from there could accommodate such phosphorylation. A very distinguishable positively charged sequence is present upstream from the tyrosine, suggesting a signal transduction system involving negatively charged phosphate groups and positively charged lysine and arginine groups.

These features of the CA125 molecule suggest a signal transduction pathway involvement in the biological function of CA125 [Fendrick JL *et al.*, CA125 phosphorylation is associated with its secretion from the WISH human amnion cell line, *Tumor Biology* 18:278-289 (1997); and Konish I *et al.*, Epidermal growth factor enhances secretion of the ovarian tumor-associated cancer antigen CA125 from the human amnion WISH cell line, *J Soc. Gynecol. Invest.* 1:89-96 (1994)]. It also reinforces the prediction of phosphorylation prior to CA125 release from the membrane surface as previously proposed [Fendrick JL *et al.*, CA125 phosphorylation is associated with its secretion from the WISH human amnion cell line, *Tumor Biology* 18:278-289 (1997); and Konish I *et al.*, Epidermal growth factor enhances secretion of the ovarian tumor-associated cancer antigen CA125 from the human amnion WISH cell line, *J Soc. Gynecol. Invest.* 1:89-96 (1994)]. Furthermore, a putative proteolytic cleavage site on the extra-cellular side of the transmembrane domain is present at position #176-181.

How well does the CA125 structure described in the present invention compare to the previously known CA125 structure? O'Brien *et al.* reported that a number of questions needed to be addressed: 1) the multivalent nature of the molecule; 2) the heterogeneity of CA125; 3) the carbohydrate composition; 4) the secretory or membrane bound nature of the CA125 molecule; 5) the function of the CA125 molecule; and 6) the elusive CA125 gene [More than 15 years of CA125: What is known about the antigen, its structure and its function, *Int J Biological Markers* 13(4)188-195 (1998)]. Several of these questions have been addressed in the present invention including, of course, the gene and its protein core product. Perhaps, most interestingly is the question of whether an individual large transcript accounted for the whole CA125 molecule, or a number of smaller

transcripts which represented subunits that specifically associated to produce the CA125 molecule. From the results produced by way of the present invention, it is now apparent that the transcript of CA125 is large - similar to some of the mucin gene transcripts e.g. MUC 5B [see Verma M *et al.*, Mucin genes: Structure, expression and regulation, *Glycoconjugate J.* 11:172-179 (1994); and Gendler SJ *et al.*, Epithelial mucin genes, *Annu. Rev. Physiol.* 57:607-634 (1995)]. The protein core extracellular domains all have a high capacity for O-glycosylation and, therefore, probably accounts for the heterogeneity of charge and size encountered in the isolation of CA125. The data also confirm the O-glycosylation inhibition data, indicating CA125 to be rich in O-glycosylation [Lloyd KO *et al.*, Synthesis and secretion of the ovarian cancer antigen CA125 by the human cancer cell line NIH: OVCAR-3, *Tumor Biology* 22, 77-82 (2001); Lloyd KO *et al.*, Isolation and characterization of ovarian cancer antigen CA125 using a new monoclonal antibody (VK-8): Identification as a mucin-type molecule, *Int. J. Cancer*, 71:842-850 (1997); and Fendrick JL *et al.*, Characterization of CA125 synthesized by the human epithelial amnion WISH cell line, *Tumor Biology* 14:310-318 (1993)].

The repeat domain which includes more than 60 repeat units accounts for the multivalent nature of the epitopes present, as each repeat unit likely contains epitope binding sites for both OC125-like antibodies and M11-like antibodies. The presence of a transmembrane domain and cleavage site confirms the membrane association of CA125, and reinforces the data which indicates a dependence of CA125 release on proteolysis. Also, the release of CA125 from the cell surface may well depend on cytoplasmic phosphorylation and be the result of EGF signaling [Nustad K *et al.*, Specificity and affinity of 26 monoclonal antibodies against the CA125 antigen: First report from the ISOBM TD-1 workshop, *Tumor Biology* 17:196-219 (1996)]. As for the question of inherent capacity of CA125 for proteolytic activity, this does not appear to be the case. However, it is likely that the associated proteins isolated along with CA125 (e.g. the 50 kDa protein which has no antibody binding ability) may have proteolytic activity. In any case, proteolysis of an extracellular cleavage site is the most likely mechanism of CA125 release. Such cleavage would be responsive to cytoplasmic signaling and mediated by an associated extracellular protease activity.

In summary, the large number of tandem repeats of the CA125 molecule, which dominate its molecular structure and contain the likely epitope binding sites of the CA125 molecule, was unexpected. Also, one cannot as yet account for the proteolytic activity, which has plagued the isolation and characterization of this molecule for many years. While no protease domain per se is constitutively part of the CA125 molecule, there is a high likelihood of a direct association by an

extracellular protease with the ligand binding domains of the CA125 molecule. Finally, what is the role of the dominant repeat domain of this extracellular structure? Based on the expression data of CA125 on epithelial surfaces and in glandular ducts, it is reasonable to conclude that the unique structure of these repeat units with their cysteine loops plays a role both as glandular anti-invasive molecules (bacterial entrapment) and/or a role in anti-adhesion (maintaining patency) between epithelial surfaces and in ductal linings.

Recently, Yin and Lloyd described the partial cloning of the CA125 antigen using a completely different approach to that described in the present invention [Yin TWT *et al.*, Molecular cloning of the CA125 ovarian cancer antigen. Identification as a new mucin (MUC16), *J Biol. Chem.* 276:27371-27375 (2001)]. Utilizing a polyclonal antibody to CA125 to screen an expression library of the ovarian tumor cell line OVCAR-3, these researchers identified a 5965 bp clone containing a stop codon and a poly A tail, which included nine partially conserved tandem repeats followed by a potential transmembrane region with a cytoplasmic tail. The 5965 bp sequence is almost completely homologous to the carboxy terminus region shown in Table 21. Although differing in a few bases, the sequences are homologous. As mentioned above, the cytoplasmic tail has the potential for phosphorylation and a transmembrane domain would anchor this part of the CA125 molecule to the surface of the epithelial or tumor cell. In the extracellular matrix, a relatively short transition domain connects the transmembrane anchor to a series of tandem repeats - in the case of Yin and Lloyd, nine.

By contrast, the major extracellular part of the molecule of the present invention as shown is upstream from the sequence described by Yin and includes a large series of tandem repeats. These results, of course, provide a different picture of the CA125 molecule, which suggest that CA125 is dominated by the series of extracellular repeats. Also included is a major amino terminal domain (~1638 amino acids) for the CA125 molecule, which it is believed accounts for a great deal of the O-glycosylation known to be an important structural component of CA125.

In conclusion, a CA125 molecule is disclosed which requires a transcript of more than 35,000 bases and occupies approximately 150,000 bp on chromosome 19q 13.2. It is dominated by a large series of extracellular repeat units (156 amino acids), which offer the potential for molecular interactions especially through a highly conserved unique cysteine loop. The repeat units also include the epitopes now well-described and classified for both the major class of CA125 antibodies (i.e., the OC125 and the M11 groups). The CA125 molecule is anchored at its carboxy terminal through a transmembrane domain and a short cytoplasmic tail. CA125 also contains a highly

glycosylated amino terminal domain, which includes a large extracellular exon typical of some mucins. Given the massive repeat domain presence of both epithelial surfaces and ovarian tumor cell surfaces, it might be anticipated that CA125 may play a major role in determining the extracellular environment surrounding epithelial and tumor cells.

5 Advantages and Uses of the CA125 Recombinant Products

1) Current assays to CA125 utilize as standards either CA125 produced from cultured cell lines or from patient ascites fluid. Neither source is defined with regard to the quality or purity of the CA125 molecule. Therefore arbitrary units are used to describe patient levels of CA125. Because cut-off values are important in the treatment of patients with elevated CA125 and because many different assay systems are used clinically to measure CA125, it is relevant and indeed necessary to define a standard for all CA125 assays. Recombinant CA125 containing epitope binding sites could fulfill this need for standardization. Furthermore, new and more specific assays may be developed utilizing recombinant products for antibody production.

2) Vaccines: Adequate data now exists [see Wagner U *et al.*, Immunological consolidation of ovarian carcinoma recurrences with monoclonal anti-idiotypic antibody ACA125: Immune responses and survival in palliative treatment, *Clin. Cancer Res.* 7:1112-1115 (2001)], which suggest and support the idea that CA125 could be used as a therapeutic vaccine to treat patients with ovarian carcinoma. Heretofore, in order to induce cellular and humoral immunity in humans to CA125, murine antibodies specific for CA125 were utilized in anticipation of patient production of anti-ideotypic antibodies, thus indirectly allowing the induction of an immune response to the CA125 molecule. With the availability of recombinant CA125, especially domains which encompass epitope binding sites for known murine antibodies and domains directly anchoring CA125 on the tumor cell, it will be feasible to more directly stimulate patients' immune systems to CA125 and as a result, extend the life of ovarian carcinoma patients as demonstrated by Wagner et al.

Several approaches can be utilized to achieve such a therapeutic response in the immune system by: 1) directly immunizing the patient with recombinant antigen containing the CA125 epitopes or other domains; 2) harvesting dendritic cells from the patient; 3) expanding these cells in *in vitro* culture; 4) activating the dendritic cells with the recombinant CA125 epitope domain or other domains or with peptides derived from these domains [see Santin AD *et al.*, Induction of

ovarian tumor-specific CD8+ cytotoxic T lymphocytes by acid-eluted peptide-pulsed autologous dendritic cells, *Obstetrics & Gynecology* 96(3):422-430 (2000)]; and then 5) returning these immune stem cells to the patient to achieve an immune response to CA125. This procedure can also be accomplished using specific peptides which are compatible with histocompatibility antigens of the patient. Such peptides compatible with the HLA-A2 binding motifs common in the population are indicated in Figure 12.

3) Therapeutic Targets: Molecules, which are expressed on the surface of tumor cells as CA125 is, offer potential targets for immune stimulation, drug delivery, biological modifier delivery or any agent which can be specifically delivered to ultimately kill the tumor cells.

CA125 offers such potential as a target: 1) Antibodies to CA125 epitopes or newly described potential epitopes: Most especially humanized or human antibodies to CA125 which could directly activate the patients' immune system to attack and kill tumor cells. Antibodies could be used to deliver all drug or toxic agents including radioactive agents to mediate direct killing of tumor cells. 2) Natural ligands: Under normal circumstances, molecules are bound to the CA125 molecule e.g. a 50 k dalton protein which does not contain CA125 epitopes co-purifies with CA125. Such a molecule, which might have a natural binding affinity for domains on the CA125 molecule, could also be utilized to deliver therapeutic agents to tumor cells.

4) Anti-sense therapy: CA125 expression may provide a survival or metastatic advantage to ovarian tumor cells as such antisense oligonucleotide derived from the CA125 sequence could be used to down-regulate the expression of CA125. Antisense therapy could be used in association with a tumor cell delivery system such as described above.

5) Small Molecules: Recombinant domains of CA125 also offer the potential to identify small molecules which bind to individual domains of the molecule. Small molecules either from combinatorial chemical libraries or small peptides can also be used as delivery agents or as biological modifiers.

All references referred to herein are hereby incorporated by reference in their entirety.

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present invention and without diminishing its attendant advantages.

TABLE 1

- 5 Comparison of the Amino Acid Terminal Sequences and Several Internal Sequences for the 40kD Band for CA125 glycoprotein (SEQ ID NO: 1 through SEQ ID NO: 4) to the Nucleotide and Amino Acid Sequences for EST Genbank Accession No. AA640762 (SEQ ID NO: 5 and SEQ ID NO: 6, respectively)

40kDa Nterm - QHPSGRKFKTTEG (SEQ ID NO: 1)

Peak 68 - FLTVERVLQGL (SEQ ID NO: 2)

Peak 65 - DTYVGPLY (SEQ ID NO: 3)

Peak 30 - DGAANGVD (SEQ ID NO: 4)

(SEQ ID NO: 5 and SEQ ID NO: 6)

1 CGTCGACCTGGCTCTAGAAAGTTTAACACCACGGAGAGAGTCCTTCAGGGTCTGCTCAGG
R R P G S R K F N T T E R V L Q G L L R

61 CCTGTGTTCAAGAACACCAAGTGTGGCCCTCTGTACTCTGGCTGCAGACTGACCTTGCTC
P V F K N T S V G P L Y S G C R L T L L

121 AGGCCCAAGAAGGATGGGGCAGCCACCAAGTGGATGCCATCTGCACCTACGCCCTGAT
R P K K D G A A T K V D A I C T Y R P D

181 CCCAAAAGCCCTGGACTGGACAGAGAGCAGCTATACTGGGAGCTGAGCCAGGGTGATGCA
P K S P G L D R E Q L Y W E L S Q G D A

TABLE 2A

5 Nucleotide and Amino Acid Sequences for Sense Primer 5' 3' (SEQ ID NO: 7 and
SEQ ID NO: 8 respectively) and Antisense Primer 5' 3'
(SEQ ID NO: 9 and SEQ ID NO: 10 respectively) based upon Regions of Homology for
EST Genbank Accession Nos. BE005912 and AA640762)

10 GGA GAG GGT TCT GCA GGG TC (SEQ ID NO: 7)

E R V L Q G (SEQ ID NO: 8)

15 GTG AAT GGT ATC AGG AGA GG (SEQ ID NO: 9)

P L L I P F (SEQ ID NO: 10)

TABLE 2B

25 Sense and Anti-Sense Primers Used for Ordering Repeat Units
(SEQ ID NO: 301 and SEQ ID NO: 302, respectively)

30 5'-GTCTCTATGTCAATGGTTTCACCC-3' (SEQ ID NO: 301)

5'-TAGCTGCTCTCTGTCCAGTCC-3' (SEQ ID NO: 302)

TABLE 3

Amino Acid Sequence for a 400 bp Repeat in the CA125 Molecule
(SEQ ID NO: 11 thru SEQ ID NO: 21)

		1			50	
	12	ERVLQGLLRS	LFKSTSVGPL	YSGCRLTLLR	PEKDGATATGV	DAICTHHHPDP (SEQ ID NO: 11)
10	34	ERVLQGLLMP	LFKNTSVSSL	YSGCRLTLLR	PEKDGAATRA	DAVCTHRPDP (SEQ ID NO: 12)
	32	ERVLQGLLGP	IFKNTSVGPL	YSGCRLTSLR	SEKDGAATGV	DAICIHRLDP (SEQ ID NO: 13)
	46	ERVLQGLLGP	MFKNTSVGLL	YSGCRLTLLR	PEKNGAATGM	DAICSHRLDP (SEQ ID NO: 14)
	33	ERVLQGLLGP	LFKNSSVGPL	YSGCRLISLR	SEKDGAATGV	DAICTHHLNP (SEQ ID NO: 15)
	15	ERVLQGLLRP	LFKSTSAGPL	YSGCRLTLLR	PEKHGAATGV	DAICTLRLDP (SEQ ID NO: 16)
15	35	ERVLQGLLKP	LFKSTSVGPL	YSGCRLTLLR	PEKRGAAATGV	DTICTHRLDP (SEQ ID NO: 17)
	111	ERVLQGLLTP	LFKNTSVGPL	YSGCRLTLLR	PEKQEAATGV	DTICTHRVDP (SEQ ID NO: 18)
	42	ERVLQGLLKP	LFKNTSVGPL	YSGCRLTLLR	PEKHEAATGV	DTICTHRLDP (SEQ ID NO: 19)
	116	ERVLQGLLSP	IFKNSSVGPL	YSGCRLTSLR	PEKDGAATGM	DAVCLYHPNP (SEQ ID NO: 20)
20	23	ERVLQGLLRP	LFKNTSIGPL	YSSCRLTLLR	PEKDKAATRV	DAICTHHHPDP (SEQ ID NO: 21)
		51			100	
	12	KSPRLDREQL	YWELSQLTHN	ITELGPYALD	NDSLTVNGFT	HRSSVSTTST
	34	KSPGLDRERL	YWKLSQLTHG	ITELGPYTLT	RHSLYVNGFT	HQSSMTTTRT
25	32	KSPGLNREQL	YWELSKLTND	IEELGPYTLT	RNSLYVNGFT	HQSSVSTTST
	46	KSPGLNREQL	YWELSQLTHG	IKELGPYTLT	RNSLYVNGFT	HRSSVAPTST
	33	QSPGLDREQL	YWQLSQMTNG	IKELGPYTLT	RNSLYVNGFT	HRSSGLTTST
	15	TGPGLDRERL	YWELSQLTNS	VTELGPYTLT	RDSLYVNGFT	HRSSVPTTSI
	35	LNPGLDREQL	YWELSKLTRG	IIELGPYTLT	RDSLYVNGFT	HRSSVPTTSI
30	111	IGPGLDRERL	YWELSQLTNS	ITELGPYTLT	RDSLYVDGFN	PWSSVPTTST
	42	LNPGLDREQL	YWELSKLTRG	IIELGPYLLD	RGSLYVNGFT	HRNFVPITST
	116	KRPGLDREQL	YWELSQLTHN	ITELGPYSLD	RDSLYVNGFT	HQNSVPTTST
	23	QSPGLNREQL	YWELSQLTHG	ITELGPYTLT	RDSLYVDGFT	HWSPIPTTST
		101			150	
35	12	PGTPTVYLGA	SKTPASIFGP	S..AASPLLI	PFT~~~~~	~~~~~
	34	PDTSTMHLAT	S RTPASLSGP	T..TASPLLI	PF~~~~~	~~~~~
	32	PGTSTVDLRT	SGTPSSLSSP	TIMAAGPLLI	PF~~~~~	~~~~~
	46	PGTSTVDLGT	SGTPSSLPSP	T..TAVPLLI	PF~~~~~	~~~~~
40	33	PWTSTVDLGT	SGTPSPVPSP	T..TAGPFLI	PF~~~~~	~~~~~
	15	PGTSAVHLET	SGTPASLPGH	T..APGPLLI	PF~~~~~	~~~~~
	35	PGTSAVHLET	SGTPASLPGH	I..VPGPLLI	PF~~~~~	~~~~~
	111	PGTSTVHLAT	SGTPSPLPGH	T..APVPLLI	PFT~~~~~	~~~~~
	42	PGTSTVHLGT	SETPSSLPRP	I..VPGPLLV	PFT~~~~~	~~~~~
	116	PGTSTVYWAT	TGTPSSFPGH	T..EPGPLLI	PF~~~~~	~~~~~
45	23	PGTSIVNLGT	SGIPPSLPET	T..ATGPLLI	PFT~~~~~	~~~~~

TABLE 3-continued

Amino Acid Sequence for a 400 bp Repeat in the CA125 Molecule
(SEQ ID NO: 11 thru SEQ ID NO: 21)

5

		151		170
10	12	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
	34	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
	32	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
	46	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
	33	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
15	15	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
	35	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
	111	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
	42	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
	116	~ ~ ~ ~ ~	~ ~ ~ ~ ~	
20	23	~ ~ ~ ~ ~	~ ~ ~ ~ ~	

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Amino Acid Sequence for a 800 bp Repeat in the CA125 Molecule
(SEQ ID NO: 22 thru SEQ ID NO: 35)

37

TABLE 4-continued

Amino Acid Sequence for a 800 bp Repeat in the CA125 Molecule
(SEQ ID NO: 22 thru SEQ ID NO: 35)

		151				200
	79	RKFNTMERVL	QGLLSPIFKN	SSVGPLYSGC	RLTSLRPEKD	GAATGMDAVC
10	811	RKFNIMERVL	QGLLMPLFKN	TSVSSLYSGC	RLTLLRPEKD	GAATRVDVAVC
	21	RKFNTTERVL	QTLLGPMFKN	TSVGLLYSGC	RLTLLRSEKD	GAATGVDAIC
	89	RKFNIMERVL	QGLLGPLFKN	SSVGPLYSGC	RLISLRSEKD	GAATGVDAIC
	85	RKFNIMERVL	QGLLNPIFKN	SSVGPLYSGC	RLTSLKPEKD	GAATGMDAVC
15	712	RKFNTTERVL	QGLLKPLFKS	TSVGPLYSGC	RLTLLRPEKR	GAATGVDTIC
	86	RKFNTTERVL	QGLLKPLFKS	TSVGPLYSGC	RLTLLRPEKR	GAATGVDTIC
	87	RKFNTTERVL	QGLLKPLFKS	TSVGPLYSGC	RLTLLRPEKH	GAATGVDAIC
	810	RKFNTMERVL	QGLLSPIFKN	SSVGPLYSGC	RLTSLRPEKD	GAATGMDAVC
	83	RKFNTATERVL	QGLLSPIFKN	SSVGPLYSGC	RLTSLRPEKD	GAATGMDAVC
20	81	RKFNIMERVL	QGLLKPLFKN	TSVGPLYSGC	RLTLLRPKKD	GAATGVDAIC
	44	RKFNTTERVL	QGLLKPLFKN	TSVGPLYSGC	RLTLLRPEKH	EAATGVDTIC
	812	RKFNTTERVL	QGLLRPVFKN	TSVGPLYSGC	RLTLLRPKKD	GAATKVDAIC
	76	RKFNTTERVL	QGLLRPVFKN	TSVGPLYSGC	RLTLLRPKKD	GAATKVDAIC
25		201				250
	79	LYHPNPKRPG	LDREQLYWEL	SQLTHNITEL	GPYSLDRDSL	YVNGFTHQNS
	811	TQRPDPKSPG	LDRERLYWKL	SQLTHGITEL	GPYTLDHRSL	YVNGFTHQSS
	21	THRLDPKSPG	VDREQLYWEL	SQLTNGIKEL	GPYTLDNRSL	YVNGFTHWIP
	89	THHLNPQSPG	LDREQLYWQL	SQMTNGIKEL	GPYTLDNRSL	YVNGFTHRSS
30	85	LYHPNPKRPG	LDREQLYWEL	SQLTHGIKEL	GPYTLDNRSL	YVNGFTHRSS
	712	THRLDPLNPG	LDREQLYWEL	SKLTRGIIEL	GPYLLDRGSL	YVNGFTHRNF
	86	THRLDPLNPG	LDREQLYWEL	SKLTRGIIEL	GPYLLDRGSL	YVNGFTHRNF
	87	THRLDPKSPG	VDREQLYWEL	SQLTNGIKEL	GPYTLDNRSL	YVNGFTHWIP
	810	LYHPNPKRPG	LDREQLY---	-----	-----	-----
35	83	LYHPNPKRPG	LDREQLYWEL	SQLTHNITEL	GPYSLDRDSL	YVNGFTHQSS
	81	THRLDPKSPG	LNREQLYWEL	SKLTNDIEEL	GPYTLDNRSL	YVNGFTHQSS
	44	THRVDPKSPG	LDRERLYWEL	SQLTNSIHEL	GPYTLDNRSL	YVNGFTHQSS
	812	TYRPDPKSPG	LDREQLYWEL	SKLTNDIEEL	GPYTLDNRSL	YVNGFTHQSS
	76	TYRPDPKSPG	LDREQLYWEL	SQLTHSITEL	GPYTQDRDSL	YVNGFTHRSS
40		251			288	
	79	VPTTSTPGTS	TVYWATTGTP	SSFPGHT..E	PGPL-----	
	811	MTTTRTPDTS	TMHLATS RTP	ASLSGPT..T	ASPLLIPF	
	21	-----	-----	-----	-----	
45	89	GLTTSTPGTS	TVDLGTSGTP	SPVPSPT..T	AGPLLIPF	
	85	VAPTSTPGTS	TVDLGTSGTP	SSLPSPT..T	AVPLLIPF	
	712	VPITSTPGTS	TVHLGTSETP	SSLPRPI..V	PGPLLIPF	
	86	VPITSTPGTS	TVHLGTSETP	SSLPRPI..V	PGPLLIPF	
	87	VPTSSTPGTS	TVDLG..SGTP	SSLPSPT..T	AGPL-----	
50	810	-----	-----	-----	-----	
	83	MTTTRTPDTS	TMHLATS RTP	ASLSGPT..T	ASPLLIPF	
	81	VSTTSTPGTS	TVDLRTSGTP	SSLSSPTIMA	AGPLLIPF	
	44	VPTTSTPGTS	TVHLATSGTP	SSLPGHT..A	PVPLLI--	
	812	VSTTSTPGTS	TVDLRTSGTP	SSLSSPTIMA	AGPLLIPF	
55	76	VPTTSIPGTS	AVHLETSGTP	ASLP-----	-----	

TABLE 5

Amino Acid Sequence for a 1200 bp Repeat in the CA125 Molecule
(SEQ ID NO: 36 thru SEQ ID NO: 46)

5

		1		50	
	910	ERVLQGLLGP	MFKNTSVGLL	YSGCRLTLLR	PEKRGAAATGV DTICTHRLDP (SEQ ID NO: 36)
10	99	ERVLHGLLTP	LFKNTRVGPL	YSGCRLTLLR	PEKQEAATGV DTICTHRVDP (SEQ ID NO: 37)
	112	-----	-----GPL	YSGCRLTSLR	PEKDGAATGM DAVCLYHPNP (SEQ ID NO: 38)
	95	ERVLQGPLSP	IFKNSSVGPL	YSGCRLTSLR	PEKDGAATGM DAVCLYHPNP (SEQ ID NO: 39)
	71	-----	-----TSVGPL	YSGCRLTLLR	SEKDGAATGV DAITYHRLDP (SEQ ID NO: 40)
	78	-----	-----	-----TLLR	PKKDGVAATGV DAICTHRLDP (SEQ ID NO: 41)
15	115	ERVLQGLLKP	LFKSTSVGPL	YSGCRLTLLR	PEKDGVAATRV DAICTHRPDP (SEQ ID NO: 42)
	91	ERVLQGLLKP	LFRNSSLEYL	YSGCRLASLR	PEKDSSAMAV DAICTHRPDP (SEQ ID NO: 43)
	92	ERVLQGLLKP	LFKSTSVGPL	YSGCRLTLLR	PEKRGAAATGV DTICTHRLDP (SEQ ID NO: 44)
	113	ERVLQGLLGP	MFKNTSVGLL	YSGCRLTLLR	PEKNGAATGM DAICSHRLDP (SEQ ID NO: 45)
	711	ERVLQGLLKP	LFKSTSVGPL	YSGCRLTLLR	PEKHGAATGV DAICTLRLDP (SEQ ID NO: 46)
20		51		100	
	910	LNPGLDREQ	YWELSKLTRG	IIELGPLYLD	RGS�YVNGFT HRNFVPITST
	99	IGPGLDRERL	YWELSQLTNS	ITELGPYTLD	RDSLYVNGFN PWSSVPTTST
25	112	KRPGLDREQ	YWELSQLTHN	ITELGPYSLD	RDSLYVNGFT HQNSVPTTST
	95	KRPGLDREQ	YWELSQLTHN	ITELGPYSLD	RDSLYVNGFT HQNSVPTTST
	71	KSPGVDREQ	YWELSQLTNG	IKELGPYTLD	RNSLYVNGFT HQTSAPNTST
	78	KSPGLNREQ	YWELSKLTND	IEELGPYTLD	RNSLYVNGFT HQSSVSTTST
	115	KIPGLDRQQL	YWELSQLTHS	ITELGPYTLD	RDSLYVNGFT QRSSVPTTST
	91	EDLGLDRERL	YWELSNLTNG	IQELGPYTLD	RNSLYVNGFT HRSSMPTTST
30	92	LNPGLDREQ	YWELSKLTRG	IIELGPLYLD	RGS�YVNGFT HRNFVPITST
	113	KSPGLNREQ	YWELSQLTHG	IKELGPYTLD	RNSLYVNGFT HRSSVAPTST
	711	TGPGLDRERL	YWELSQLTNS	VTELGPYTLD	RDSLYVNGFT HRSSVPTTSI
35		101		150	
	910	PGTSTVHLGT	SETPSSLPRP	IV..PGPLLV	PFTLNFTITN LQYEEAMRHP
	99	PGTSTVHLAT	SGTPSSLPGH	TA..PVPLLI	PFTLNFTITN LHYEENMQHP
	112	PGTSTVYAT	TGTPSSFPGH	T..EPGPLLI	PFTLNFTITN LQYEEAMGHP
	95	PGTSTVYAT	TGTPSSFPGH	T..EPGPLLI	PFTLNFTITN LQYEEAMGHP
	71	PGTSTVDLGT	SGTPSSLPSP	T..SAGPLLI	PFTINFTITN LRYEENMHHP
40	78	PGTSTVDLRT	SGTPSSLSP	TIMAAGPLLI	PFTINFTITN LRYEENMHHP
	115	PGTFTVQPET	SETPSSLPGP	T..ATGPVLL	PFTLNFTIIN LQYEEDMHRP
	91	PGTSTVDVGT	SGTPSSSPSP	T..TAGPLLM	PFTLNFTITN LQYEEDMRRT
	92	PGTSTVHLGT	SETPSSLPRP	IV..PGPLLI	PFTLNFTITN LQYEEAMGHP
	113	PGTSTVDLGT	SGTPSSLPSP	T..TAVPLLI	PFTLNFTITN LKYEEDMHCP
45	711	PGTSAVHLET	SGTPASLPGH	T..APGPLLI	PFTLNFTITN LHYEENMQHP
50		151		200	
	910	GSRKFNTER	VLQGLLRPLF	KNTSVSSLYS	GCRLTLLRPE KDGAATRVDA
	99	GSRKFNTER	VLQGLLKPLF	KNTSVGPLY	GCRLTLFKPE KHEAATGVDA
	112	GSRKFNTER	VLQGLLTPLF	KNSSVGPLY	GCRLISLRSE KDGAATGVDA
	95	GSRKFNTER	VLQGLLNPIF	KNSSVGPLY	GCRLTSLRPE KDGAATGVDA
	71	GSRKFNTER	VLQGLLKPLF	KSTSVGPLY	GCRLTLLRPE KDGVAATRVDA
	78	GSRKFNTER	VLQGLLMPLF	KNTSVSSLYS	GCRLTLLRPE KDGAATRVDA
	115	GSRKFNTER	VLQGLLMPLF	KNTSVGPLY	GCRLTLLRPE KQEAATGVDT
55	91	GSRKFNTER	VLQGLLKPLF	KNTSVGPLY	GCRLTLLRPE KDGAATGVDA
	92	GSRKFNTER	VLQGLLKPLF	RNSSLEYLYS	GCRLTSLRPE KDSSTMAVDA

TABLE 5-continued

Amino Acid Sequence for a 1200 bp Repeat in the CA125 Molecule
(SEQ ID NO: 36 thru SEQ ID NO: 46)

5

113 GSRKFNTTER VLQSLFGPMF KNTSVGPLYG GCRLTLFRSE KDGAATGVDA
711 GSRKFNTMER VLQGCCLVPCS RNTNVGLLYS GCRLTLLXXX XXXXXXXXXXXX

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201 250
910 ACTYRPDPKS PGLDREQLYW ELSQLTHSIT ELGPYTLDRV SLYVNGFNPR
99 ICTLRDPTG PGLDRERLYW ELSQLTNSVT ELGPYTLDRD SLYVNGFTHR
112 ICTHHLNPQS PGLDREQLYW QLSQMTNGIK ELGPYTLDRD SLYVNGFTHR
15 95 VCLYHPNPKR PGLDREQLYC ELSQLTHNIT ELGPYSLDRD SLYVNGFTHQ
71 ICTHRPDPKI PGLDRQQLYW ELSQLTHSIT ELGPYTLDRD SLYVNGFTQR
78 VCTHRPDPKS PGLDRERLYW KLSQLTHGIT ELGPYTLDRN SLYVNGFTHR
115 ICTHRLDPSE PGLDREQLYW ELSQLTNSIT ELGPYTLDRD SLYVNGFTHS
91 ICTHRLDPKS PGLNREQLYW ELSKLTNDIE EVGPYTLDRN SLYVNGFTHR
20 92 ICTHRPDPED LGLDRERLYW ELSNLTNGIQ ELGPYTLDRN SLYVNGFTHR
113 ICTHRLDPKS PGVDREQLYW ELSQLTNGIK ELGPYTLDRN SLYVNGFTHQ
711 XXXXXXXXXXXX XXXXXXXXXXXX XXXXXXXXXXXX XXGPYTLDRN SLYVNGFTHR

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251 300
910 SSV.PTTSTP GTSTVHLATS GTPSSLPGHT APVPLLIPFT LNFTITNLQY
99 SSV.PTTSIP GTSVHLETS GTPASLPGHT APGPLLIPFT LNFTITNLQY
112 SL.GLTTSTP WTSTVDLGTS GTPSPVPSPT TAGPLLIPFT LNFTITNLQY
95 NS.VPTTSTP GTSTVYWATT GTPSSFPGHT EPGPLLIPFT LNFTITNLQY
71 SSV.PTTSTP GTFTVQPETS ETPSSLPGPT ATGPVLLPFT LNFTIINLQY
300 78 SSM.PTTSTP GTSTVDVGTS GTPSSSPSPT TAGPLLMPFT LNFTITNLQY
115 GVLCPPPSIL GIFTVQPETF ETPSSLPGPT ATGPVLLPFT LNFTIINLQY
91 SFVAP.TSTL GTSTVDLGTS GTPSSLPSPT TGVPLLIPFT LNFTITNLQY
92 SFM.PTTSTL GTSTVDVGTS GTPSSSPSPT TAGPLLMPFT LNFTITNLQY
350 113 TS.APNTSTP GTSTVDLGTS GTPSSLPSPT SAGPLLVPFT LNFTITNLQY
711 SSVAP.TSTP GTSTVDLGTS GTPSSLPSPT TV.PLLVPFT LNFTITNLQY

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301 350
910 EEDMRHPGSR KFNTMERVLQ GLLRPLFKNT SIGPLYSSCR LTLLRPEKDK
99 EEDMRRTGSR KFNTMERVLQ GLLKPLFKST SVGPLYSGCR LTLLRPEKRG
112 EENMGHPGSR KFNIMERVLQ GLLRPVFKNT SVGPLYSGCR LTLLRPPKDG
95 EEDMRRTGSR KFNTMERVLQ GLLKPLFKST SVGPLYSGCR LTLLRPEKHG
71 EEDMRHPGSR KFNTTERVLQ GLLKPLFKST SVGPLYSGCR LTLLRPEKHG
78 EEDMRRTGSR KFNTMERVLQ GLLKPLFKST SVGPLYSGCR LTLLRPEKHG
115 EEDMRHPGSR KFNTERVLQ GLLMPLFKNT SVGPLYSGCR LTLLRPEKQE
45 91 EENMGHPGSR KFNIMERVLQ GLLMPLFKNT SVSSLYSGCR LTLLRPEKDG
92 EEDMRRTGSR KFNTMESVLQ GLLKPLFKNT SVGPLYSGCR LTLLRPPKDG
113 EEDMRRTGSR KFNTMESVLQ GLLKPLFKNT SVGPLYSGCR LTLLRPEKDG
711 GEDMRHPGSR KFNTTERVLQ GLLGPLFKNS SVGPLYSGCR LISLRSEKDG

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351 400
910 AATRVDIAICT HHPDPQSPGL NREQLYWELS QLTHGITEL~ ~~~~~
99 AATGVDTICT HRLDPLNPGL DREQLYWELS KLTRGIIELG PYLLDRGSLY
112 AATKVDAICT YRPDPKSPGL DREQLYWELS QLTHSITELG PYTLDRDSLY
95 AATGVDAICT LRLDPTGPGL DRERLYWELS QLTNSVTELG PYTLDRDSLY
55 71 AATGVDAICT LRLDPTGPGL DRERLYWELS QLTNSITELG PYTLDRDSLY
78 AATGVDAICT LRLDPTGPGL DRERLYWELS QLTNSVTELG PYTLDRDSLY

TABLE 5-continued

Amino Acid Sequence for a 1200 bp Repeat in the CA125 Molecule
(SEQ ID NO: 36 thru SEQ ID NO: 46)

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115 AATGVDICT HRVDPKSPGL DRERLYWELS QLNSITELG PYTLDRDSLY
 91 AATRVVAVCT HRPDPKSPGL DRERLYWKLS QLTHGITELG PYTLDRHSLY
 92 AATGVDAICT HRLDPKSPGL NREQLYWELS KLTNDIEELG PYTLDRNSLY
 113 AATGVDAICT HRLDPKSPGL NREQLYWELS KL-----
 711 AATGVDAICT HHLNPQSPGL DREQLYWQLS QVTNGIKELG PYTLDRNSLY

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910 -----
 99 VNGFTHRNFV PITSTPGTST VHLGTSEIHP SLPRPI..VP GPL-----
 112 VNGFTQRSSV PTTSTPGTPT VDLGTSGTPV SKPGPS..AA SP-----
 95 VNGFTHRSSV PTTSTPGTSA VHLETSGTPA SLPGHT..AP GPLL---
 71 VNGFNPWSSV PTTSTPGTST VHLATSGTPS SLPGHT..AP VPL-----
 78 VNGFTHRSSV PTTSTPGTSA VHLETSGTPA SLPGHT..AP GPLLIPF
 115 VNGFNPWSSV PTTSTPGTST VHLATSGTPS SLPGHT..AP VPLLIPF
 91 VNGFTHQSSM TTTSTPDTST MHLATSRTPA SLSGPT..TA SPLLI--
 92 VNGFTHQSSV STTSTPGTST VDPRTSGTPS SLSSPTIMAA GPLLI--
 113 -----
 711 VNGFTHRSSG LTTSTPWTST VDLGTSGTPS PVPSPT..TA GPLLI--

TABLE 6

Amino Acid Sequence for a 9 Repeat Structure in the CA125 Molecule
(SEQ ID NO: 47)

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ERV LQGLLKP LFRNSSLEYL YSGCRLASLR PEKDSSAMAV DAICTHRDPD
EDLGLDRERL YWELSNLTNG IQELGPYTLD RNSLYVNGFT HRSSMPTTST
PGTSTVDVGT SGTPSSSSPSP TTAGPLLMPF TLNFTITNLQ YEEDMRRTGS
RKFNTMERVL QGPLSPIFKN SSVGPLYSGC RLTSRPEKD GAATGM DAV
CLYHPNPKRP GLDREQLYWE LSQLTHNITE LGPYSLDRDS LYVNGFTHQN
SVPTTSTPGT STVYWATTGT PSSFPGHTEP GPLLIPFTLN FTITNLQYEE
NMGHPGSRKF NITERVLQGL LNPIFKNSSV GPLYSGCRLT SLRPEKDGA
TGMDAVCLYH PNPKRPGLD R EQLYCELSQL THNITELGPY SLDRDSLYVN
GFTHQNSVPT TSTPGTSTVY WATTGTPSSF PGHTEPGPLL IPFTLNFTIT
NLQYEEDMR TGSRKFNTE RVLQGLLKPL FKSTSVGPLY SGCRLTLLRP
EKHGAATGVD AICTLRDPT GPGLDRERLY WELSQLTNSV TELGPYTLD
DSLYVNGFTH RSSVPTTSIP GTSAVHLETS GTPASLP GHT APGPLLVPFT
LNFTITNLQY EEDMRHPGSR KFNTTERVLQ GLLKPLFKST SVGPLYSGCR
LTLRPEKRG AATGVDICT HRLDPLNPGL DREQLYWELS KLTRGIIELG
PYLLDRGSLY VNGFTHRN FV PITSTPGTST VHLGTSETPS SLPRPIVPGP
LLIPFTLNFT ITNLQYEENM GHPSRKFN I TERNVQGLLK PLFRNSSLEY
LYSGCRLASL RPEKDSSAMA VDAICTHRDP PEDLGLDRER LYWELSNLTN
GIQELGPYTL DRNSLYVNGF THRSSMPTTS TPGTSTVDVG TSGTPSSSSPS
PTTAGPLLMP FTLNFTITNL QYEEDMRRTG SRKFNTMESV LQGLLKPLFK
NTSVGPLYSG CRLTLLRPKK DGAATGVDAI CTHRLDPKSP GLNREQLYWE
LSKLTNDIEE VGPYTLD RNS LYVNGFTHRS FVAPTSTLGT STVDLGTSGT
PSSLPSPTTG VPLLIPFTLN FTITNLQYEE NMGHPGSRKF NIMERVLQGL
LSPIFKNSSV GSPLYSGCRLT LLRPEKDGA TRVDAVCTHR PDPKSPGLDR
ERLYWKLSQL THGIIELGPY TLD RHSFYVN GFTHQSSMTT TRTPDTSTMH
LATSRTPASL SGPTTASPLL VLFTINF TIT NQRYEENMH PGSRKFNTTE
RVLQGLLRPV FKNTSVGPLY SGCRLTLLRP KKDGAATKVD AICTYRPDPK
SPGLDREQLY WELSQLTHSI TELGPYTQDR DSYLVNGFTH RSSVPTTSIP
GTSAVHLETS GTPASLP

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TABLE 7

cDNA Genbank Accession # AK024365 Encompasses Repeat Sequences (Repeats 1 & 2)
 Homologous to Two Repeats Shown in Table 6
 (SEQ ID NO: 48)

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10	MPLFKNTSVS	SLYSGCRLTL	LRPEKDGAAT	RVDAVCTHRP	DPKSPGLDRE
	RLYWKLSQLT	HGIIELGPYT	LDRHSFYVNG	FTHQSSMTT	RTPDTSTMHL
	ATSRTPASLS	GPTTASPLL	LFTINFITN	QRYEENMHHP	GSRKFNTER
	VLQGLLRPVF	KNTSVGPLY	GCRLTLLRPK	KDGAATKVDA	ICTYRPDPKS
	PGLDREQLYW	ELSQLTHSIT	ELGPYTQDRD	SLYVNGFTHR	SSVPTTSIPG
	TSVHLETSG	TPASLPGPSA	ASPLLVLFTL	NFTITNLRYE	ENMQHPGSRK
15	FNTTERVLQG	LLRSLFKSTS	VGPLYSGCRL	TLLRPEKDG	ATGVDAICTH
	HPDPKSPRLD	REQLYWELSQ	LTHNITELGH	YALDNDLSFV	NGFTHRSSVS
	TTSTPGTPTV	YLGASKTPAS	IFGPSAASHL	LILFTLNFTI	TNLRYEENMW
	PGSRKFNTTE	RVLQGLLRPL	FKNTSVGPLY	SGSRLTLLRP	EKDGEATGVD
	AICTHRPDPT	GPGLDREQLY	LELSQLTHSI	TELGPYTLDR	DSLYVNGFTH
20	RSSVPPTSTG	VVSEEPFTLN	FTINNLRMA	DMGQPGSLKF	NITDNVMKHL
	LSPLFQSSSL	GARYTGCRVI	ALRSVKNGAE	TRVDLLCTYL	QPLSGPGLPI
	KQVFHELSQL	THGITRLGPY	SLDKDSLYLN	GYNEPGLDEP	PTTPKPATTF
	LPPLSEATTA	MGYHLKTLTL	NFTISNLQYS	PDMGKGSATF	NSTEGVLQHL
	LRPLFQKSSM	GPFYLGCLLI	SLRPEKDGA	TGVDTTCTYH	PDPVGPGLDI
25	QQLYWELSQL	THGVTQLGFY	VLDKDSLFIN	GYAPQNLIR	GEYQINFHIV
	NWNLSNPDPT	SSEYITLLRD	IQDKVTTLK	GSQHDTRFR	CLVTNLTMD
	VLVTVKALFS	SNLDPSLVEQ	VFLDKTLNAS	FHWLGSTYQL	VDIHVTEMES
	SVYQPTSSSS	TQHFYLNFTI	TNLPYSQDKA	QPGTTNYQRN	KRNIEDALNQ
	LFRNSSIKSY	FSDCQVSTFR	SVPNRHHTGV	DSLGNFSPLA	RRVDRVAIYE
30	EFLRMTRNGT	QLQNFLLDRS	SVLVDGYSPN	RNEPLTGNSD	LPFWAVILIG
	LAGLLGLITC	LICGVLVTTR	RRKKEGEYNV	QQQCPGYYS	HLDLEDLQ

TABLE 8

Complete DNA Sequence for 13 Repeats including the Carboxy Terminus of CA125
(SEQ ID NO: 49)

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1  GAGAGGGTTC TGCAGGGTCT GCTCAAACCC TTGTTTCAGGA ATAGCAGTCT
51  GGAATACCTC TATTCAGGCT GCAGACTAGC CTCACTCAGG CCAGAGAAGG
101 ATAGCTCAGC CATGGCAGTG GATGCCATCT GCACACATCG CCCTGACCCT
151 GAAGACCTCG GACTGGACAG AGAGCGACTG TACTGGGAGC TGAGCAATCT
201 GACAAATGGC ATCCAGGAGC TGGGCCCCCTA CACCCTGGAC CGGAACAGTC
251 TCTATGTCAA TGGTTTCACC CATCGAAGCT CTATGCCCAC CACCAGCACT
301 CCTGGGACCT CCACAGTGGA TGTGGGAACC TCAGGGACTC CATCCTCCAG
351 CCCCAGCCCC ACGACTGCTG GCCCTCTCCT GATGCCGTTC ACCCTCAACT
401 TCACCATCAC CAACCTGCAG TACGAGGAGG ACATGCGTCG CACTGGCTCC
451 AGGAAGTTCA ACACCATGGA GAGGGTTCTG CAGGGTCCGC TTAGTCCCAT
501 ATTCAAGAAC TCCAGTGTTG GCCCTCTGTA CTCTGGCTGC AGACTGACCT
551 CTCTCAGGCC CGAGAAGGAT GGGGCAGCAA CTGGAATGGA TGCTGTCTGC
601 CTCTACCACC CTAATCCCAA AAGACCTGGG CTGGACAGAG AGCAGCTGTA
651 CTGGGAGCTA AGCCAGCTGA CCCACAACAT CACTGAGCTG GGCCCCTACA
701 GCCTGGACAG GGACAGTCTC TATGTCAATG GTTTCACCCA TCAGAACTCT
751 GTGCCCACCA CCAGTACTCC TGGGACCTCC ACAGTGTA CT GGGCAACCAC
801 TGGGACTCCA TCCTCCTTCC CCGGCCACAC AGAGCCTGGC CCTCTCCTGA
851 TACCATTAC GCTCAACTTC ACCATCACTA ACCTACAGTA TGAGGAGAAC
901 ATGGGTCACC CTGGCTCCAG GAAGTTCAAC ATCACGGAGA GGGTTCTGCA
951 GGGTCTGCTT AATCCCATT TCAAGAACTC CAGTGTGGC CCTCTGTACT
1001 CTGGCTGCAG ACTGACCTCT CTCAGGCCCG AGAAGGATGG GGCAGCAACT
1051 GGAATGGATG CTGTCTGCCT CTACCACCCT AATCCCAGAA GACCTGGGCT
1101 GGACAGAGAG CAGCTGTACT GCGAGCTAAG CCAGCTGACC CACAACATCA
1151 CTGAGCTGGG CCCCTACAGC TTGGACAGGG ACAGTCTTTA TGTCAATGGT

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TABLE 8-continued

Complete DNA Sequence for 13 Repeats including the Carboxy Terminus of CA125
(SEQ ID NO: 49)

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1201 TTCACCCATC AGAACTCTGT GCCCACCACC AGTACTCCTG GGACCTCCAC
 1251 AGTGTACTGG GCAACCACTG GGACTCCATC CTCCTTCCCC GGCCACACAG
 1301 AGCCTGGCCC TCTCCTGATA CCATTACCCC TCAACTTCAC CATCACCAAC
 1351 CTGCAGTACG AGGAGGACAT GCGTCGCACT GGCTCCAGGA AGTTCAACAC
 1401 CATGGAGAGG GTTCTGCAGG GTCTGCTCAA GCCCTTGTTT AAGAGCACCA
 1451 GCGTTGGCCC TCTGTACTCT GGCTGCAGAC TGACCTTGCT CAGACCTGAG
 1501 AAACATGGGG CAGCCACTGG AGTGGACGCC ATCTGCACCC TCCGCCTTGA
 1551 TCCCACTGGT CCTGGACTGG ACAGAGAGCG GCTATACTGG GAGCTGAGCC
 1601 AGCTGACCAA CAGCGTTACA GAGCTGGGCC CCTACACCCT GGACAGGGAC
 1651 AGTCTCTATG TCAATGGCTT CACCCATCGG AGCTCTGTGC CAACCACCAG
 1701 TATTCCTGGG ACCTCTGCAG TGCACCTGGA AACCTCTGGG ACTCCAGCCT
 1751 CCCTCCCTGG CCACACAGCC CCTGGCCCTC TCCTGGTGCC ATTCACCCTC
 1801 AACTTCACTA TCACCAACCT GCAGTATGAG GAGGACATGC GTCACCCTGG
 1851 TTCCAGGAAG TTCAACACCA CGGAGAGAGT CCTGCAGGGT CTGCTCAAGC
 1901 CCTTGTTCAA GAGCACCAGT GTTGGCCCTC TGTA CTCTGG CTGCAGACTG
 1951 ACCTTGCTCA GGCCTGAAAA ACGTGGGGCA GCCACCGGCG TGGACACCAT
 2001 CTGCACTCAC CGCCTTGACC CTCTAAACCC TGGACTGGAC AGAGAGCAGC
 2051 TATACTGGGA GCTGAGCAAA CTGACCCGTG GCATCATCGA GCTGGGCCCC
 2101 TACCTCCTGG ACAGAGGCAG TCTCTATGTC AATGGTTTCA CCCATCGGAA
 2151 CTTTGTGCCC ATCACCAGCA CTCCTGGGAC CTCCACAGTA CACCTAGGAA
 2201 CCTCTGAAAC TCCATCCTCC CTACCTAGAC CCATAGTGCC TGGCCCTCTC
 2251 CTGATACCAT TCACACTCAA CTTACCATC ACTAACCTAC AGTATGAGGA
 2301 GAACATGGGT CACCCTGGCT CCAGGAAGTT CAACATCACG GAGAGGGTTC
 2351 TGCAGGGTCT GCTCAAACCC TTGTTTCAGGA ATAGCAGTCT GGAATACCTC

TABLE 8-continued

Complete DNA Sequence for 13 Repeats including the Carboxy Terminus of CA125
(SEQ ID NO: 49)

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2401 TATTCAGGCT GCAGACTAAC CTCACTCAGG CCAGAGAAGG ATAGCTCAAC
 2451 CATGGCAGTG GATGCCATCT GCACACATCG CCCTGACCCT GAAGACCTCG
 2501 GACTGGACAG AGAGCGACTG TACTGGGAGC TGAGCAATCT GACAAATGGC
 2551 ATCCAGGAGC TGGGCCCCTA CACCCTGGAC CGGAACAGTC TCTATGTCAA
 2601 TGGTTTCACC CATCGAAGCT CTATGCCAC CACCAGCACT CCTGGGACCT
 2651 CCACAGTGGA TGTGGGAACC TCAGGGACTC CATCCTCCAG CCCAGCCCC
 2701 ACGACTGCTG GCCCTCTCCT GATGCCGTTT ACCCTCAACT TCACCATCAC
 2751 CAACCTGCAG TACGAGGAGG ACATGCGTCG CACTGGCTCC AGGAAGTTCA
 2801 ACACCATGGA GAGTGTCTTG CAGGGTCTGC TCAAGCCCTT GTTCAAGAAC
 2851 ACCAGTGTG GCCCTCTGTA CTCTGGCTGC AGATTGACCT TGCTCAGGCC
 2901 CAAGAAAGAT GGGGCAGCCA CTGGAGTGGA TGCCATCTGC ACCCACCGCC
 2951 TTGACCCCAA AAGCCCTGGA CTCAACAGGG AGCAGCTGTA CTGGGAGTTA
 3001 AGCAAACTGA CCAATGACAT TGAAGAGGTG GGCCCTACA CCTTGGACAG
 3051 GAACAGTCTC TATGTCAATG GTTTCACCCA TCGGAGCTTT GTGGCCCCCA
 3101 CCAGCACTCT TGGGACCTCC ACAGTGGACC TTGGGACCTC AGGGACTCCA
 3151 TCCTCCCTCC CCAGCCCCAC AACAGGTGTT CCTCTCCTGA TACCATTAC
 3201 ACTCAACTTC ACCATCACTA ACCTACAGTA TGAGGAGAAC ATGGGTCACC
 3251 CTGGCTCCAG GAAGTTCAAC ATCATGGAGA GGGTTCTGCA GGGTCTGCTT
 3301 ATGCCCTTGT TCAAGAACAC CAGTGTGAGC TCTCTGTACT CTGGTTGCAG
 3351 ACTGACCTTG CTCAGGCCTG AGAAGGATGG GGCAGCCACC AGAGTGGTTG
 3401 CTGTCTGCAC CCATCGTCCT GACCCCAAAA GCCCTGGACT GGACAGAGAG
 3451 CGGCTGTACT GGAAGCTGAG CCAGCTGACC CACGGCATCA CTGAGCTGGG
 3501 CCCCTACACC CTGGACAGGC ACAGTCTCTA TGTCAATGGT TTCACCCATC
 3551 AGAGCTCTAT GACGACCACC AGAACTCCTG ATACCTCCAC AATGCACCTG

TABLE 8-continued

Complete DNA Sequence for 13 Repeats including the Carboxy Terminus of CA125
(SEQ ID NO: 49)

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3601 GCAACCTCGA GAACTCCAGC CTCCTGTCT GGACCTACGA CCGCCAGCCC
3651 TCTCCTGATA CCATTCACAA TTAACCTCAC CATCACTAAC CTGCGGTATG
3701 AGGAGAACAT GCATCACCTT GGCTCTAGAA AGTTTAACAC CACGGAGAGA
3751 GTCCTTCAGG GTCTGCTCAG GCCTGTGTTC AAGAACACCA GTGTTGGCCC
3801 TCTGTACTCT GGCTGCAGAC TGACCTTGCT CAGGCCCAAG AAGGATGGGG
3851 CAGCCACCAA AGTGGATGCC ATCTGCACCT ACCGCCCTGA TCCCAAAGC
3901 CCTGGACTGG ACAGAGAGCA GCTATACTGG GAGCTGAGCC AGCTAACCCA
3951 CAGCATCACT GAGCTGGGCC CCTACACCCT GGACAGGGAC AGTCTCTATG
4001 TCAATGGTTT CACACAGCGG AGCTCTGTGC CCACCACTAG CATTCCTGGG
4051 ACCCCCACAG TGGACCTGGG AACATCTGGG ACTCCAGTTT CTAAACCTGG
4101 TCCCTCGGCT GCCAGCCCTC TCCTGGTGCT ATTCACTCTC AACTTCACCA
4151 TCACCAACCT GCGGTATGAG GAGAACATGC AGCACCTGG CTCCAGGAAG
4201 TTCAACACCA CGGAGAGGGT CCTTCAGGGC CTGCTCAGGT CCCTGTTCAA
4251 GAGCACCAGT GTTGGCCCTC TGTA CTCTGG CTGCAGACTG ACTTTGCTCA
4301 GGCCTGAAAA GGATGGGACA GCCACTGGAG TGGATGCCAT CTGCACCCAC
4351 CACCCTGACC CCAAAGCCC TAGGCTGGAC AGAGAGCAGC TGTATTGGGA
4401 GCTGAGCCAG CTGACCCACA ATATCACTGA GCTGGGCCAC TATGCCCTGG
4451 ACAACGACAG CCTCTTTGTC AATGGTTTCA CTCATCGGAG CTCTGTGTCC
4501 ACCACCAGCA CTCCTGGGAC CCCACAGTG TATCTGGGAG CATCTAAGAC
4551 TCCAGCCTCG ATATTGGGCC CTTAGCTGC CAGCCATCTC CTGATACTAT
4601 TCACCCTCAA CTTACCATC ACTAACCTGC GGTATGAGGA GAACATGTGG
4651 CCTGGCTCCA GGAAGTTCAA CACTACAGAG AGGGTCCTTC AGGGCCTGCT
4701 AAGGCCCTTG TTCAAGAACA CCAGTGTGG CCCTCTGTAC TCTGGCTCCA
4751 GGCTGACCTT GCTCAGGCCA GAGAAAGATG GGAAGCCAC CGGAGTGGAT

TABLE 8-continued

Complete DNA Sequence for 13 Repeats including the Carboxy Terminus of CA125
(SEQ ID NO: 49)

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4801 GCCATCTGCA CCCACCGCCC TGACCCACACA GGCCCTGGGC TGGACAGAGA
 4851 GCAGCTGTAT TTGGAGCTGA GCCAGCTGAC CCACAGCATC ACTGAGCTGG
 4901 GCCCCTACAC ACTGGACAGG GACAGTCTCT ATGTCAATGG TTTCACCCAT
 4951 CGGAGCTCTG TACCCACCAC CAGCACCGGG GTGGTCAGCG AGGAGCCATT
 5001 CACACTGAAC TTCACCATCA ACAACCTGCG CTACATGGCG GACATGGGCG
 5051 AACCCGGCTC CCTCAAGTTC AACATCACAG ACAACGTCAT GAAGCACCTG
 5101 CTCAGTCCTT TGTTCAGAG GAGCAGCCTG GGTGCACGGT ACACAGGCTG
 5151 CAGGGTCATC GACTAAGGT CTGTGAAGAA CGGTGCTGAG ACACGGGTGG
 5201 ACCTCCTCTG CACCTACCTG CAGCCCCTCA GCGGCCCAGG TCTGCCTATC
 5251 AAGCAGGTGT TCCATGAGCT GAGCCAGCAG ACCCATGGCA TCACCCGGCT
 5301 GGGCCCCTAC TCTCTGGACA AAGACAGCCT CTACCTTAAC GGTTACAATG
 5351 AACCTGGTCT AGATGAGCCT CCTACAATC CCAAGCCAGC CACCACATTC
 5401 CTGCCTCCTC TGTCAGAAGC CACAACAGCC ATGGGGTACC ACCTGAAGAC
 5451 CCTCACACTC AACTTCACCA TCTCCAATCT CCAGTATTCA CCAGATATGG
 5501 GCAAGGGCTC AGCTACATTC AACTCCACCG AGGGGGTCCT TCAGCACCTG
 5551 CTCAGACCCT TGTTCAGAA GAGCAGCATG GGCCCTTCT ACTTGGGTGG
 5601 CCAACTGATC TCCCTCAGGC CTGAGAAGGA TGGGGCAGCC ACTGGTGTGG
 5651 ACACCACCTG CACCTACCAC CCTGACCCTG TGGGCCCCGG GCTGGACATA
 5701 CAGCAGCTTT ACTGGGAGCT GAGTCAGCTG ACCCATGGTG TCACCCAACT
 5751 GGGCTTCTAT GTCCTGGACA GGGATAGCCT CTTTATCAAT GGCTATGCAC
 5801 CCCAGAATTT ATCAATCCGG GGCGAGTACC AGATAAATTT CCACATTGTC
 5851 AACTGGAACC TCAGTAATCC AGACCCACACA TCCTCAGAGT ACATCACCTT
 5901 GCTGAGGGAC ATCCAGGACA AGGTCACCAC ACTCTACAAA GGCAGTCAAC
 5951 TACATGACAC ATTCCGCTTC TGCCTGGTCA CCAACTTGAC GATGGACTCC

TABLE 8-continued

Complete DNA Sequence for 13 Repeats including the Carboxy Terminus of CA125
(SEQ ID NO: 49)

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6001 GTGTTGGTCA CTGTCAAGGC ATTGTTCTCC TCCAATTGG ACCCCAGCCT
6051 GGTGGAGCAA GTCTTTCTAG ATAAGACCCT GAATGCCTCA TTCCATTGGC
6101 TGGGCTCCAC CTACCAGTTG GTGGACATCC ATGTGACAGA AATGGAGTCA
6151 TCAGTTTATC AACCAACAAG CAGCTCCAGC ACCCAGCACT TCTACCCGAA
6201 TTTCACCATC ACCAACCTAC CATATTCCCA GGACAAAGCC CAGCCAGGCA
6251 CCACCAATTA CCAGAGGAAC AAAAGGAATA TTGAGGATGC GCTCAACCAA
6301 CTCTTCCGAA ACAGCAGCAT CAAGAGTTAT TTTTCTGACT GTCAAGTTTC
6351 AACATTCAGG TCTGTCCCCA ACAGGCACCA CACCGGGGTG GACTCCCTGT
6401 GTAACTTCTC GCCACTGGCT CGGAGAGTAG ACAGAGTTGC CATCTATGAG
6451 GAATTTCTGC GGATGACCCG GAATGGTACC CAGCTGCAGA ACTTCACCCT
6501 GGACAGGAGC AGTGTCTTG TGGATGGGTA TTCTCCCAAC AGAAATGAGC
6551 CCTTAACTGG GAATTCTGAC CTTCCCTTCT GGGCTGTCAT CTTTCATCGG
6601 TTGGCAGGAC TCCTGGGACT CATCACATGC CTGATCTGCG GTGTCCTGGT
6651 GACCACCCGC CGGCGGAAGA AGGAAGGAGA ATACAACGTC CAGCAACAGT
6701 GCCCAGGCTA CTACCAGTCA CACCTAGACC TGGAGGATCT GCAATGACTG
6751 GAACTTGCCG GTGCCTGGGG TGCCTTTCCC CCAGCCAGGG TCCAAAGAAG
6801 CTTGGCTGGG GCAGAAATAA ACCATATTGG TCG

TABLE 9

Complete Amino Acid Sequence for 13 Repeats Contiguous with the Carboxy Terminus
of CA125 (SEQ ID NO: 50)

1
ERVLQGLLKP LFRNSSLEYL YSGCRLASLR PEKDSSAMAV DAICTHRPDP

10
EDLGLDRERL YWELSNLTNG IQELGPYTLN RNSLYVNGFT HRSSMPTTST
PGTSTVDVGT SGTPTSSSPSP TTAGPLLMPF TLNFTITNLQ YEEDMRRTGS

15
2
RKFNMTMERVL QGPLSPIFKN SSVGPLYSGC RLTSRLRPEKD GAATGMDAVC
LYHPNPKRPG LDREQLYWEL SQLTHNITEL GPYSLDRDSL YVNGFTHQNS
VPTTSTPGTS TVYWATTGTP SSFPGHTEPG PLLIPFTLNF TITNLQYEEN

20
3
MGHPGSRKFN ITERVLQGLL NPIFKNSSVG PLYSGCRLTS LRPEKDGAAT
GMDAVCLYHP NPKRPGLDRE QLYCELSQLT HNITELGPYS LDRDSLYVNG
FTHQNSVPTT STPGTSTVYW ATTGTPSSFP GHTEPGPLLI PFTLNFTITN

25
4
LQYEEDMRRT GSRKFNTMER VLQGLLKPLF KSTSVGPLYG GCRLTLLRPE
KHGAATGVDA ICTLRLDPTG PGLDRERLYW ELSQLTNSVT ELGPYTLDRD
SLYVNGFTHR SSVPTTSIPG TSAVHLETSG TPASLPGHTA PGPLLVPFTL

30
5
NFTITNLQYE EDMRHGSRK FNTTERVLQG LLKPLFKSTS VGPLYSGCRL
TLLRPEKRG AATGVDITICHT RLDPLNPGLD REQLYWELSK LTRGIIELGP

35
6
YLLDRGSLYV NGFTHRNFPV ITSTPGTSTV HLGTSPTSS LPRPIVPGPL
LIPFTLNFTI TNLQYEENMG HPGSRKFNT ERVLQGLLKP LFRNSSLEYL

40
7
YSGCRLASLR PEKDSSAMAV DAICTHRPDP EDLGLDRERL YWELSNLTNG
IQELGPYTLN RNSLYVNGFT HRSSMPTTST PGTSTVDVGT SGTPTSSSPSP
TTAGPLLMPF TLNFTITNLQ YEEDMRRTGS RKFNMTMESVL QGLLKPLFKN

45
8
TSVGPLYSGC RLTLRPPKD GAATGVDAIC THRLDPKSPG LNREQLYWEL
SKLTNDIEEV GPYTLDRNSL YVNGFTHRSF VAPTSTLGTS TVDLGTSPTG
SSLPSTTGV PLLIPFTLNF TITNLQYEEN MGHPGSRKFN IMERVLQGLL

50
9
SPIFKNSSVG SLYSGCRLTL LRPEKDGAAT RVDVCTHRP DPKSPGLDRE
RLYWKLSQLT HGIIELGPYT LDRHSFYVNG FTHQSSMTT RTPDTSTMHL

55
10
ATSRTPASLS GPTTASPLL LFTINFTITN QRYEENMHHP GSRKFNTTER

TABLE 9-continued

Complete Amino Acid Sequence for 13 Repeats Contiguous with the Carboxy Terminus
of CA125 (SEQ ID NO: 50)

5

9

VLQGLLRPVF KNTSVGPLY GCRLTLLRPK KDGAATKVDA ICTYRPDPKS

10

PGLDREQLYW ELSQLTHSIT ELGPYTQDRD SLYVNGFTHR SSVPTTSIPG

TSAVHLETSG TPASLPGPSA ASPLLVLFTL NFTITNLRYE ENMQHPGSRK

10

FNTTTERVLQG LLRSLFKSTS VGPLYSGCRL TLLRPEKDGT ATGVDAICTH

15

HPDPKSPRLD REQLYWELSQ LTHNITELGH YALDNDSLFV NGFTHRSSVS

TTSTPGTPTV YLGASKTPAS IFGPSAASHL LILFTLNFTI TNLRYEENMW

11

20

PGSRKFNTTE RVLQGLLRPL FKNTSVGPLY SGSRLTLLRP EKDGEATGVD

AICTHRPDPT GPGLDREQLY LELSQLTHSI TELGPYTLDR DSLYVNGFTH

RSSVPTTSTG VVSEEPFTLN FTINNLRYMA DMGQPGSLKF NITDNVMKHL

12

LSPLFQRSSL GARYTGCRVI ALRSVKNGAE TRVDLLCTYL QPLSGPGLPI

KQVFHELSQL THGITRLGPY SLDKDSLYLN GYNEPGLDEP PTPPKPATTF

LPPLSEATTA MGYHLKTLTL NFTISNLQYS PDMGKSATF NSTEGLVQLHL

13

LRPLFQKSSM GPFYLG~~C~~QLI SLRPEKDGA TGVDTTCTYH PDPVGPGLDI

QQLYWELSOL THGVTQLGFY VLD~~R~~SLFIN GYAPQNL~~S~~IR GEYQINFHIV

NWNLSNPDPPT SSEYITLLRD IQDKVTTLYK GSQLHDTFRF CLVTNLTMDS

VLVTVKALFS SNLDPSLVEQ VFLDKTLNAS FHWLGSTYQL VDIHVTEMES

40

SVYQPTSSSS TQHFYLNFTI TNLPYSQDKA QPGTTNYQRN KRNIEDALNQ

LFRNSSIKSY FSDCQVSTFR SVPNRHHTGV DSLCNFSPLA RRVD~~R~~VAIYE

EFLRMTRNGT QLQNF~~T~~LD~~R~~S SVLVDGYSPN RNEPLTGNSD LPFWAVILIG

45

LAGLLGLITC LICGVLVTTR R~~R~~KKEGEYNV QQCPGYYQS HLDLEDLQ

50

TABLE 10A

5' Primer Sequence for End of the Open Reading Frame for Contig #32 of Chromosome
 19 Cosmid AC008734 (SEQ ID NO: 51), Primer Sequence from within the Repeat Region
 (SEQ ID NO: 52, 3 Primer Sets Synthesized to Piece Together Entire Open Reading
 Frame in Contig #32 (SEQ ID NOS: 53 thru 58), Primers to Cosmid No. AC008734 for
 Contig #32 (SEQ ID NOS: 59 and 60), Sense Primer Sequence (supplied by Ambion)
 (SEQ ID NO: 61), Anti-Sense Primer Sequence for CA125 (SEQ ID NO: 62), and
 5' Sense Primer Sequence (from Ambion) (SEQ ID NO: 63) and Anti-Sense Primer
 Specific to CA125 (SEQ ID NO: 64)

(SEQ ID NO: 51) (5'-CAGCAGAGACCAGCACGAGTACTC-3')

(SEQ ID NO: 52) (5'-TCCACTGCCATGGCTGAGCT-3')

Primer Sets

(SEQ ID NO: 53) (Set 1) 5'-CCAGCACAGCTCTTCCCAGGAC-3'
 (SEQ ID NO: 54) 5'-GGAATGGCTGAGCTGACGTCTG-3')

(SEQ ID NO: 55) (Set 2) 5'-CTTCCCAGGACAACCTCAAGG-3'
 (SEQ ID NO: 56) 5'-GCAGGATGAGTGAGCCACGTG-3')

(SEQ ID NO: 57) (Set 3) 5'-GTCAGATCTGGTGACCTCACTG-3'
 (SEQ ID NO: 58) 5'-GAGGCACTGGAAAGCCCAGAG-3')

(SEQ ID NO: 59) 5'-CTGATGGCATTATGGAACACATCAC-3'
 (SEQ ID NO: 60) 5'-CCCAGAACGAGAGACCAGTGAG-3'

(SEQ ID NO: 61) 5'-GCTGATGGCGATGAATGAACACTG-3'

(SEQ ID NO: 62) 5'-CCCAGAACGAGAGACCAGTGAG-3'

(SEQ ID NO: 63) 5'-CGCGGATCCGAACACTGCGTTTGCTGGCTTTGATG-3'

(SEQ ID NO: 64) 5'-CCTCTGTGTGCTGCTTCATTGGG-3'

TABLE 10B

Sense and Anti-Sense Primers Used to Order the CA125 Carboxy Terminal Domain
(SEQ. ID NO: 303 and SEQ ID NO: 304, respectively)

(SEQ ID NO: 303) 5'-GGACAAGGTCACCACTCTAC-3'
(SEQ ID NO: 304) 5'-GCAGATCCTCCAGGTCTAGGTGTG-3'

TABLE 10C

Sense and Anti-Sense Primers Used to Amplify Overlapping Sequences
in the Repeat Domain
(SEQ ID NO: 305 and SEQ ID NO: 306, respectively)

(SEQ ID NO: 305) 5' GTC TCT ATG TCA ATG GTT TCA CCC-3'
(SEQ ID NO: 306) 5'-TAG CTG CTC TCT GTC CAG TCC-3'

TABLE 11

5' Sense Primer 1 Sequence and 3' Antisense Primer 2
(SEQ ID NO: 65 and SEQ ID NO: 66, respectively), and
Nucleotide and Amino Acid Sequences of the CA125 Repeat Expressed in *E. coli*
(SEQ ID NO: 67 and SEQ ID NO: 68, respectively)

10 (SEQ ID NO: 65) 5'-ACCGGATCCATGGGCCACACAGAGCCTGGCCC-3'

(SEQ ID NO: 66) 5'-TGTAAGCTTAGGCAGGGAGGATGGAGTCC-3'

(SEQ ID NO: 67)

15
1 ATGAGAGGAT CGCATCACCA TCACCATCAC GGATCCATGG GCCACACAGA
51 GCCTGGCCCT CTCCTGATAC CATTCACTTT CAACTTTACC ATCACCAACC
20 101 TGCATTATGA GGAAAACATG CAACACCCTG GTTCCAGGAA GTTCAACACC
151 ACGGAGAGGG TTCTGCAGGG TCTGCTCAAG CCCTTGTTCA AGAACACCAG
201 TGTGAGCCCT CTGTACTCTG GCTGCAGACT GACCTTGCTC AGACCTGAGA
25 251 AGCATGAGGC AGCCACTGGA GTGGACACCA TCTGTACCCA CCGCGTTGAT
301 CCCATCGGAC CTGGACTGGA CAGAGAGCGG CTATACTGGG AGCTGAGCCA
30 351 GCTGACCAAC AGCATCACAG AGCTGGGACC CTACACCCTG GACAGGGACA
401 GTCTCTATGT CAATGGCTTC AACCTCGGA GCTCTGTGCC AACCACCAGC
451 ACTCCTGGGA CCTCCACAGT GCACCTGGCA ACCTCTGGGA CTCCATCCTC
35 501 CCTGCCT

(SEQ ID NO: 68)

40 M R G S H H H H H G S M G H T E P G P L L I P F T F N F T I T N L
H Y E E N M Q H P G S R K F N T T E R V L Q G L L K P L F K N T S V
G P L Y S G C R L T L L R P E K H E A T G V D T I C T H R V D P I
G P G L D R E R L Y W E L S Q L T N S I T E L G P Y T L D R D S L Y
45 V N G F N P R S S V P T T S T P G T S T V H L A T S G T P S S L P

TABLE 12

Additional Multiple Repeat Amino Acid Sequences
(SEQ ID NO: 69 thru SEQ ID NO: 80)

(SEQ ID NO: 69)

10 ERVLQGLLGP MFKNTSVGLL YSGCRLTLRL PKKDGAATKV DAICTYRPDP
KSPGLDREQL YWELSQLTHS ITELGPYTLR RDSLYVNGFT QRSSVPTTSI
15 PGTPVDLGT SGTPVSKPGP SAASPLLIPF TINFITNLRL YEENMGHPGS
RKFNIMERVL QGLLKPLFKN TSVGPLYSGC RLTLRLPKKD GAATGVDAIC
THRLDPKSPG LNREQLYWEL SKLTNDIEEL GPYTLDRNSL YVNGFTHQSS
20 VSTTSTPGTS TVDLRTSGTP SSLSSPTIMA AGPLLIPFTI NFITNLRLYE
ENMHHPGSRK FNTMERVLQG LLMPPLFKNTS VSSLYSGCRL TLRLPEKDGA
25 ATRVDAVCTH RPDPKSPGLD RERLYWKLK LTHGITELGP YTLDRNSLYV
NGFTHRSSMP TTSTPGTSTV DVGTSCTPSS SPSPTTAGPL LMPFTLNFTI
TNLQYEDMR RTGSRKFNTM ERVLQGLLKP LFKSTSVGPL YSGCRLTLRL
30 PEKHGAATGV DAICTLRLDP TGPGLDRERL YWELSQLTNS VTELGPYTLR
RDSLYVNGFT HRSSVPTTSI PGTSVHLET SGTPASLPGH TAPGPLLIPF
TLNFTITNLH YEENMQHPGS RKFNIMERVL QGCLVPCSRN TNVGLLYSGC
35 RLTLRLXKX XAATXVDXXC XXXXDPXXPG LDREXLYWEL SXLTXIXEL
GPYTLDRNSL YVNGFTHRSS VAPTSTPGTS TVDLGTSGTP SSLPSPTTVP
40 LLVPFTLNFT ITNLQYGEDM RHGSRKFNT TERVLQGLLG PLFKNSSVGP
LYSGCRLISL RSEKDGAATG VDAICTHHLN PQSPGLDREQ LYWQLSQVTN
45 GIKELGPYTL DRNSLYVNGF THRSSGLTTS TPWTSTVDLG TSGTPSPVPS
PTTAGPLLI

TABLE 12-continued

Additional Multiple Repeat Amino Acid Sequences
(SEQ ID NO: 69 through SEQ ID NO: 80)

(SEQ ID NO: 70)

10 QGLLGPMFKN TSVGLLYSGC RLTLLRPEKR GAATGVD TIC THRLDPLNPG
LDREQLYWEL SKLTRGIIEI GPYLLDRGSL YVNGFTHRNF VPITSTPGTS
TVHLGTSETP SSLPRPIVPG PLLVPFTLNF TITNLQYEEA MRHPGSRKFN
15 TTERVLQGLL RPLFKNTSVS SLYSGCRLTL LRPEKDGAAT RVDAACTYRP
DPKSPGLDRE QLYWELSQLT HSITELGPYT LDRVSLYVNG FNPRSSVPTT
20 STPGTSTVHL ATSGTPSSLP GHTAPVPLLI PFTLNFTITN LQYEEDMRHP
GSRKFNTMER VLQGLLRPLF KNTSIGPLYS SCRLTLLRPE KDKAATR VDA
ICTHHPDPQS PGLNREQLYW ELSQLTHGIT ELGPYTLDRD SLYVDGFTHW
25 SPIPTTSTPG TSIVNLGTSG IPPSLPETTA TGPLLIPFTP NFTITNLQYE
EDMRRTGSRK FNTMERVLQG LLSPIFKNSS VGPLYSGCRL TSLRPEKDGA
30 ATGMDAVCLY HPNPKRPGLD REQLY

(SEQ ID NO: 71)

35 ERVLQGLLKP LFKSTSVGPL YSGCRLTLLR PEKDG VATRV DAICTHRPDP
KIPGLDRQQI YWELSQTLS ITELGPYTLD RDSLYVNGFT QRSSVPTTST
PGTFTVQPET SETPSSLPGP TATGPVLLPF TLNFTIINLQ YEEDMRHPGS
40 RKFNTTERVL QGLLMPLFKN TSVGPLYSGC RLTLLRPEKQ EAATGVD TIC
THRLDPSEPG LDREQLYWEL SQLTNSITEL GPYTLDRDSL YVNGFTHSGV
45 LCPPPSILGI FTVQPETFET PSSLPPTAT GPVLLPFTLN FTIINLQYEE
DMHRPGSRKF NTTERVLQGL LTPLFKNTSV GPLYSGCRLT LLRPEKQ EAA
TGVD TIC THR VDPGPGGLDR ERLYWELSQT TNSITELGPY TLDRLSYVN
50 GFNPWSSVPT TSTPGTSTVH LATSGTPSSL PGHTAPVPLL IPFTLNFTIT

TABLE 12-continued

Additional Multiple Repeat Amino Acid Sequences
(SEQ ID NO: 69 through SEQ ID NO: 80)

NLHYEENMQH PGSRKFNTE RVLQGLLKPL FKSTSVGPLY SGCRLTLLRP
 EKHGAAATGVD AICTHRLDPK SPGVDREQLY WELSQLTNGI KELGPYTLDR
 NSLYVNGFTH WIPVPTSSTP GTSTVDLGSG TPSSLPSPTT AGPL

(SEQ ID NO: 72)

TSVGPLYSGC RLTLLRSEKD GAATGVDAIY THRLDPKSPG VDREQLYWEL
 SQTNGIKEL GPYTLDRNSL YVNGFTHQTS APNTSTPGTS TVDLGTSGTP
 SSLPSPTSAG PLLIPFTINF TITNLRYEEN MHPGSRKFN TMERVLQGLL
 KPLFKSTSVG PLYSGCRLTL LRPEKDG VAT RVDAICTHRP DPKIPGLDRQ
 QLYWELSQLT HSITELGPYT LDRDSLYVNG FTQRSSVPTT STPGTFTVQP
 ETSETPSSLP GPTATGPVLL PFTLNFTIIN LQYEEDMHRP GSRKFNTTER
 VLQGLLKPLF KSTSVGPLY SGCRLTLLRPE KHGAATGVDA ICTLRLDPTG
 PGLDRERLYW ELSQLTNSIT ELGPYTLDRD SLYVNGFNPW SSVPTTSTPG
 TSTVHLATSG TPSSLPGHTA PVPL

(SEQ ID NO: 73)

ERVLQGLLKPL LFKSTSVGPLY YSGCRLTLLR PEKGAATGV DTICTHRLDP
 LNPGLDREQL YWELSKLTRG IIELGPYLLD RDSLYVNGFT HRSSVPTTSI
 PGTSAVHLET SGTPASLP GH TAPGPLLVPF TLNFTITNLQ YEEDMRHPGS
 RKFNTERVL QGLLKPLFKS TSVGPLYSGC RLTLLRPEKR GAATGVD TIC
 THRLDPLNPG LDREQLYWEL SKLTRGIEL GPYLLDRGSL YVNGFTHRNF
 VPITSTPGTS TVHLGTSETP SSLPRPIVPG PLLIPF

TABLE 12-continued

Additional Multiple Repeat Amino Acid Sequences
(SEQ ID NO: 69 through SEQ ID NO: 80)

(SEQ ID NO: 74)

10 ERVLQGLLRP VFKNTSVGPL YSGCRLTLR PKKGAATKV DAICTYRDPD
KSPGLDREQL YWELSQLTHS ITELGPYTL D RSLYVNGFT QRSSVPTTSI
PGTPTVDLGT SGTPVSKPGP SAASPLLVPF TLNFTITNLQ YEEDMHRPGS
15 RKFNATERVL QGLLSPIFKN SSVGPLYSGC RLTSLRPEKD GAATGMDAVC
LYHPNPKRPG LDREQLYWEL SQLTHNITEL GPYSLDRDSL YVNGFTHQSS
20 MTTTRTPDTS TMHLATS RTP ASLSGPTTAS PLLIPF

(SEQ ID NO: 75)

25 ERVLQGLLKP LFKSTSVGPL YSGCRLTLR PEKGAATGV DTICTHRLDP
LNPGLDREQL YWELSKLTRG IIELGPYLLD RGS LYVNGFS RQSSMTTTRT
PDTSTMHLAT SRTPASLSGP TTASPLLIPF TLNFTITNLQ YEENMGHPGS
30 RKFNIMERVL QGLLNPIFKN SSVGPLYSGC RLTSLKPEKD GAATGMDAVC
LYHPNPKRPG LDREQLYWEL SQLTHGIKEL GPYTLDRNSL YVNGFTHRSS
35 VAPTSTPGTS TVDLGTSGTP SSLPSPTTAV PLLIPF

(SEQ ID NO: 76)

40 ERVLQGLLKP LFRNSSLEYL YSGCRLASL PEKDSSAMAV DAICTHRPDP
EDLGLDRERL YWELSNLTNG IQELGPYTL D RNSLYVNGFT HRSSGLTTST
PWTSTVDLGT SGTPSPVPSP TTAGPLLIPF TLNFTITNLQ YEENMGHPGS
45 RKFNIMERVL QGLLMPLFKN TSVSSLYSGC RLTLLRPEKD GAATRVDAVC
TQRDPKSPG LDRERLYWKL SQLTHGITEL GPYTLDRHSL YVNGLTHQSS
50 MTTTRTPDTS TMHLATS RTP ASLSGPTTAS PLLIPF

TABLE 12-continued

Additional Multiple Repeat Amino Acid Sequences
(SEQ ID NO: 69 through SEQ ID NO: 80)

(SEQ ID NO: 77)

10 ERVLQGLLSP ISKNSSVGPL YSGCRLTSLR PEKDGAATGM DAVCLYHPNP
KRPGLDREQ L YWELSQLTHN ITELGPYSLD RDSLYVNGFT HQNSVPTTST
PGTSTVIWAT TGTSSFPFGH TEPGPLLIPF TVNFTITNLR YEENMHHPGS
15 RKFNTERVL QGLLRPVFKN TSVGPLYSGC RLTLRPPKD GAATKVDAIC
TYRDPKSPG LDREQLYWEL SKLTNDIEEL GPYTLDRNSL YVNGFTHQSS
20 VSTTSTPGTS TVDLRTSGTP SSLSSPTIMA AGPLLIPF

(SEQ ID NO: 78)

25 ERVLHGLLTP LFKNTRVGPL YSGCRLTLR PEKQEAATGV DTICTHRVDP
IGPGLDRERL YWELSQLTNS ITELGPYTL D RDSLYVNGFN PWSSVPTTST
PGTSTVHLAT SGTPSSLPGH TAPVPLLIPF TLNFTITNLH YEENMQHPGS
30 RKFNTERVL QGLLKPLFKN TSVGPLYSGC RLTLFKPEKH EAATGVDAIC
TLRLDPTGPG LDRQLYWELS QLTNSVTELG PYTLDRDSLY VNGFTHRSSV
PTTSIPG TSA VHLETSGTPA SLPGHTAPGP LLIPFTLNFT ITNLQYEEDM
35 RRTGSRKFNT MERV LQGLLK PLFKSTSVGP LYSGCRLTLL RPEKGAATG
VDICTHRLD PLNPGLDREQ LYWELSKLTR GIELGPYLL DRGSLYVNGF
40 THRNFPITS TPGTSTVHLG TSETPSSLPR PIVPGPLLIP FTINFTITNL
RYEENMHHPG SRKFNIMERV LQLLGPLFK NSSVGPLYSG CRLISLRSEK
DGAATGVDAI CTHHLNPQSP GLDREQLYWQ LSQMTNGIKE LGPYTLDRNS
45 LYVNGFTHRS SGLTTSTPWT STVDLGTSGT PSPVPSPTTA GPLLIPF

50

TABLE 12-continued

Additional Multiple Repeat Amino Acid Sequences
(SEQ ID NO: 69 through SEQ ID NO: 80)

(SEQ ID NO: 79)

5
10
15
20
25
30
35
40
45
50

GPLYSGCRLT SLRPEKDGAA TGMDAVCLYH PNPKRPGGLDR EQLYWELSQL
THNITELGPY SLDRDSLYVN GFTHQNSVPT TSTPGTSTVY WATTGTPSSF
PGHTEPGPLL IPFTLNFTIT NLQYEENMGH PGSRKFNITE SVLQGLLTPL
FKNSSVGPLY SGCRLISLRS EKDGAATGVD AICTHHLNPQ SPGLDREQLY
WQLSQMTNGI KELGPYTLDR DSLYVNGFTH RSLGLTTSTP WTSTVDLGT
GTPSPVPSPT TAGPLLIPFT LNFTITNLQY EENMGHPGSR KFNIMERVLO
GLLRPVFKNT SVGPLYSGCR LTLRLPKKDG AATKVDAICT YRPDPKSPGL
DREQLYWELS QLTHSITELG PYTLDRDSLY VNGFTQRSSV PTTSIPGTPT
VDLGTSGTPV SKPGPSAASP

(SEQ ID NO: 80)

QLYWELSKLT NDIEELGPYT LDRNSLYVNG FTHQSSVSTT STPGTSTVDL
RTSGTPSSLS SPTIMAAGPL LIPFTLNFTI TNLQYEENMG HPGSRKFNIM
ERVLQGLLGP MFKNTSVGLL YSGCRLTLR PEKNGAATGM DAICSHRLDP
KSPGLNREQ L YWELSQLTHG IKELGPYTLDRNSLYVNGFT HRSSVAPTST
PGTSTVDLGT SGTPSSLPS TTA VPLLIPF TLNFTITNLK YEEDMHCPGS
RKFNTERVL QSLFGPMFKN TSVGPLYSGC RLTLRSEKD GAATGVDAIC
THRLDPKSLG VDREQLYWEL SQLTNGIKEL GPYTLDRNSL YVNGFTHQTS
APNTSTPGTS TVDLGTSGTP SSLPSPTSAG PLLVPFTLNF TITNLQYEED
MRRTGSRKFN TMESVLQGLL KPLFKNTSVG PLYSGCRLTL LRPEKDGAAT
GVDAICTHRL DPKSPGLNRE QLYWELSKL

TABLE 13

Amino Terminal Nucleotide Sequence
(SEQ ID NO: 81)

1 CAGAGAGCGT TGAGCTGGGA ACAGTGACAA GTGCTTATCA AGTTCCTTCA
51 CTCTCAACAC GGTGACAAG AACTGATGGC ATTATGGAAC ACATCACAAA
101 AATACCCAAT GAAGCAGCAC ACAGAGGTAC CATAAGACCA GTCAAAGGCC
151 CTCAGACATC CACTTCGCCT GCCAGTCCTA AAGGACTACA CACAGGAGGG
15 201 ACAAAAAGAA TGGAGACCAC CACCACAGCT TTGAAGACCA CCACCACAGC
251 TTTGAAGACC ACTTCCAGAG CCACCTTGAC CACCAGTGTC TATACTCCCA
301 CTTTGGGAAC ACTGACTCCC CTCAATGCAT CAAGGCAAAT GGCCAGCACA
351 ATCCTCACAG AAATGATGAT CACAACCCCA TATGTTTTCC CTGATGTTCC
401 AGAAACGACA TCCTCATTGG CTACCAGCCT GGGAGCAGAA ACCAGCACAG
25 451 CTCTTCCCAG GACAACCCCA TCTGTTCTCA ATAGAGAATC AGAGACCACA
501 GCCTCACTGG TCTCTCGTTC TGGGGCAGAG AGAAGTCCGG TTATTCAAAC
30 351 TCTAGATGTT TCTTCTAGTG AGCCAGATAC AACAGCTTCA TGGGTTATCC
601 ATCCTGCAGA GACCATCCCA ACTGTTTCCA AGACAACCCC CAATTTTTTC
651 CACAGTGAAT TAGACACTGT ATCTTCCACA GCCACCAGTC ATGGGGCAGA
35 701 CGTCAGCTCA GCCATTCCAA CAAATATCTC ACCTAGTGAA CTAGATGCAC
751 TGACCCCACT GGTCATTATT TCGGGGACAG ATACTAGTAC AACATTCCCA
40 801 AACTGACTA AGTCCCCACA TGAAACAGAG ACAAGAACCA CATGGCTCAC
851 TCATCCTGCA GAGACCAGCT CAACTATTCC CAGAACAATC CCCAATTTTT
901 CTCATCATGA ATCAGATGCC ACACCTTCAA TAGCCACCAG TCCTGGGGCA
45 951 GAAACCAGTT CAGCTATTCC AATTATGACT GTCTCACCTG GTGCAGAAGA

TABLE 13-continued

		Amino Terminal Nucleotide Sequence (SEQ ID NO: 81)					
5		1001	TCTGGTGACC	TCACAGGTCA	CTAGTTCTGG	GACAGACAGA	AATATGACTA
10		1051	TTCCAAC TTT	GACTCTTTCT	CCTGGTGAAC	CAAAGACGAT	AGCCTCATTA
		1101	GTCACCCATC	CTGAAGCACA	GACAAGTTCG	GCCATTCCAA	CTTCAACTAT
		1151	CTCGCCTGCT	GTATCACGGT	TGGTGACCTC	AATGGTCACC	AGTTTGGCGG
15		1201	CAAAGACAAG	TACAACTAAT	CGAGCTCTGA	CAAAC TCCCC	TGGTGAACCA
		1251	GCTACAACAG	TTTCATTGGT	CACGCATCCT	GCACAGACCA	GCCCAACAGT
20		1301	TCCCTGGACA	ACTTCCATTT	TTTTCCATAG	TAAATCAGAC	ACCACACCTT
25		1351	CAATGACCAC	CAGTCATGGG	GCAGAATCCA	GTTCAGCTGT	TCCAAC TCCA
		1401	ACTGTTTCAA	CTGAGGTACC	AGGAGTAGTG	ACCCCTTTGG	TCACCAGTTC
		1451	TAGGGCAGTG	ATCAGTACAA	CTATTCCAAT	TCTGACTCTT	TCTCCTGGTG
		1501	AACCAGAGAC	CACACCTTCA	ATGGCCACCA	GTCATGGGGA	AGAAGCCAGT
30		1551	TCTGCTATT C	CAACTCCAAC	TGTTTCACCT	GGGGTACCAG	GAGTGGTGAC
		1601	CTCTCTGGTC	ACTAGTTCTA	GGGCAGTGAC	TAGTACAAC T	ATTCCAATTC
		1651	TGACTTTTTTC	TCTTGGTGAA	CCAGAGACCA	CACCTTCAAT	GGCCACCAGT
35		1701	CATGGGACAG	AAGCTGGCTC	AGCTGTTCCA	ACTGTTTTTAC	CTGAGGTACC
		1751	AGGAATGGTG	ACCTCTCTGG	TTGCTAGTTC	TAGGGCAGTA	ACCAGTACAA
40		1801	CTCTTCCAAC	TCTGACTCTT	TCTCCTGGTG	AACCAGAGAC	CACACCTTCA
		1851	ATGGCCACCA	GTCATGGGGC	AGAAGCCAGC	TCAACTGTTC	CAACTGTTTC
		1901	ACCTGAGGTA	CCAGGAGTGG	TGACCTCTCT	GGTCACTAGT	TCTAGTGGAG
45		1951	TAAACAGTAC	AAGTATTCCA	ACTCTGATT C	TTTCTCCTGG	TGAACTAGAA

TABLE 13-continued

5	Amino Terminal Nucleotide Sequence (SEQ ID NO: 81)	
10	2001 ACCACACCTT CAATGGCCAC CAGTCATGGG GCAGAAGCCA GCTCAGCTGT	
	2051 TCCAACCTCA ACTGTTTCAC CTGGGGTATC AGGAGTGGTG ACCCCTCTGG	
	2101 TCACTAGTTC CAGGGCAGTG ACCAGTACAA CTATTCCAAT TCTAACTCTT	
	2151 TCTTCTAGTG AGCCAGAGAC CACACCTTCA ATGGCCACCA GTCATGGGGT	
15	2201 AGAAGCCAGC TCAGCTGTTC TAACTGTTTC ACCTGAGGTA CCAGGAATGG	
	2251 TGACCTCTCT GGTCAGTAGT TCTAGAGCAG TAACCAGTAC AACTATTCCA	
20	2301 ACTCTGACTA TTTCTTCTGA TGAACCAGAG ACCACAACCTT CATTGGTCAC	
	2351 CCATTCTGAG GCAAAGATGA TTTCAGCCAT TCCAACCTTA GCTGTCTCCC	
	2401 CTACTGTACA AGGGCTGGTG ACTTCACTGG TCACTAGTTC TGGGTCAGAG	
25	2451 ACCAGTGCGT TTTCAAATCT AACTGTTGCC TCAAGTCAAC CAGAGACCAT	
	2501 AGACTCATGG GTCGCTCATC CTGGGACAGA AGCAAGTTCT GTTGTTCCAA	
30	2551 CTTTGACTGT CTCCACTGGT GAGCCGTTTA CAAATATCTC ATTGGTCACC	
	2601 CATCCTGCAG AGAGTAGCTC AACTCTTCCC AGGACAACCT CAAGGTTTTC	
	2651 CCACAGTGAA TTAGACACTA TGCCTTCTAC AGTCACCAGT CCTGAGGCAG	
35	2701 AATCCAGCTC AGCCATTTCA ACTACTATTT CACCTGGTAT ACCAGGTGTG	
	2751 CTGACATCAC TGGTCACTAG CTCTGGGAGA GACATCAGTG CAACTTTTCC	
40	2801 AACAGTGCCT GAGTCCCCAC ATGAATCAGA GGCAACAGCC TCATGGGTTA	
	2851 CTCATCCTGC AGTCACCAGC ACAACAGTTC CCAGGACAAC CCCTAATTAT	
	2901 TCTCATAGTG AACCAGACAC CACACCATCA ATAGCCACCA GTCCTGGGGC	
45	2951 AGAAGCCACT TCAGATTTTC CAACAATAAC TGTCTCACCT GATGTACCAG	

TABLE 13-continued

5	Amino Terminal Nucleotide Sequence (SEQ ID NO: 81)					
10	3001	ATATGGTAAC	CTCACAGGTC	ACTAGTTCTG	GGACAGACAC	CAGTATAACT
	3051	ATTCCAACTC	TGA CTCTTTC	TTCTGGTGAG	CCAGAGACCA	CAACCTCATT
	3101	TATCACCTAT	TCTGAGACAC	ACACAAGTTC	AGCCATTCCA	ACTCTCCCTG
15	3151	TCTCCCCTGG	TGCATCAAAG	ATGCTGACCT	CACTGGTCAT	CAGTTCTGGG
	3201	ACAGACAGCA	CTACAACTTT	CCCAACACTG	ACGGAGACCC	CATATGAACC
	3251	AGAGACAACA	GCCATACAGC	TCATTCATCC	TGCAGAGACC	AACACAATGG
20	3301	TTCCAAGAC	AACTCCAAG	TTTTCCCATA	GTAAGTCAGA	CACCACACTC
	3351	CCAGTAGCCA	TCACCAGTCC	TGGGCCAGAA	GCCAGTTCAG	CTGTTTCAAC
	3401	GACAACTATC	TCACCTGATA	TGTCAGATCT	GGTGACCTCA	CTGGTCCCTA
25	3451	GTTCTGGGAC	AGACACCAGT	ACAACCTTCC	CAACATTGAG	TGAGACCCCA
	3501	TATGAACCAG	AGACTACAGT	CACGTGGCTC	ACTCATCCTG	CAGAAACCAG
30	3551	CACAACGGTT	TCTGGGACAA	TTCCAACCTT	TTCCCATAGG	GGATCAGACA
	3601	CTGCACCCTC	AATGGTCACC	AGTCCTGGAG	TAGACACGAG	GTCAGGTGTT
	3651	CCAAC TACAA	CCATCCCACC	CAGTATACCA	GGGGTAGTGA	CCTCACAGGT
35	3701	CACTAGTTCT	GCAACAGACA	CTAGTACAGC	TATTCCA ACT	TTGACTCCTT
	3751	CTCCTGGTGA	ACCAGAGACC	ACAGCCTCAT	CAGCTACCCA	TCCTGGGACA
40	3801	CAGACTGGCT	TCACTGTTCC	AATTCGGACT	GTTCCCTCTA	GTGAGCCAGA
	3851	TACAATGGCT	TCCTGGGTCA	CTCATCCTCC	ACAGACCAGC	ACACCTGTTT
	3901	CCAGAACAAC	CTCCAGTTTT	TCCCATAGTA	GTCCAGATGC	CACACCTGTA
45	3951	ATGGCCACCA	GTCCTAGGAC	AGAAGCCAGT	TCAGCTGTAC	TGACAACAAT

TABLE 13-continued

5	Amino Terminal Nucleotide Sequence (SEQ ID NO: 81)					
10	4001	CTCACCTGGT	GCACCAGAGA	TGGTGACTTC	ACAGATCACT	AGTTCTGGGG
	4051	CAGCAACCAG	TACAACTGTT	CCAACTTTGA	CTCATTCTCC	TGGTATGCCA
15	4101	GAGACCACAG	CCTTATTGAG	CACCCATCCC	AGAACAGGGA	CAAGTAAAC
	4151	ATTTCTGCT	TCAACTGTGT	TTCCTCAAGT	ATCAGAGACC	ACAGCCTCAC
20	4201	TCACCATTAG	ACCTGGTGCA	GAGACTAGCA	CAGCTCTCCC	AACTCAGACA
	4251	ACATCCTCTC	TCTTCACCCT	ACTTGTA ACT	GGAACCAGCA	GAGTTGATCT
25	4301	AAGTCCA ACT	GCTTCACCTG	GTGTTTCTGC	AAAAACAGCC	CCACTTTCCA
	4351	CCCATCCAGG	GACAGAGACC	AGCACAATGA	TTCCA ACTTC	AACTCTTTCC
30	4401	CTTGTTTAC	TAGAGACTAC	AGGCTTACTG	GCCACCAGCT	CTTCAGCAGA
	4451	GACCAGCACG	AGTACTCTAA	CTCTGACTGT	TTCCCCTGCT	GTCTCTGGGC
35	4501	TTTCAGTGC	CTCTATAACA	ACTGATAAGC	CCCAA ACTGT	GACCTCCTGG
	4551	AACACAGAAA	CCTCACCATC	TGTA ACTTCA	GTTGGACCCC	CAGAATTTTC
40	4601	CAGGACTGTC	ACAGGCACCA	CTATGACCTT	GATACCATCA	GAGATGCCAA
	4651	CACCACCTAA	AACCAGTCAT	GGAGAAGGAG	TGAGTCCAAC	CACTATCTTG
45	4701	AGAACTACAA	TGTTGAAGC	CACTAATTTA	GCTACCACAG	GTTCCAGTCC
	4751	CACTGTGGCC	AAGACAACAA	CCACCTTCAA	TACTGTGGCT	GGAAGCCTCT
50	4801	TACTCCTCT	GACCACACCT	GGGATGTCCA	CCTTGGCCTC	TGAGAGTGTG
	4851	ACCTCAAGAA	CAAGTTATAA	CCATCGGTCC	TGGATCTCCA	CCACCAGCAG
55	4901	TTATAACCGT	CGGTACTGGA	CCCCTGCCAC	CAGCACTCCA	GTGACTTCTA
	4951	CATTCTCCCC	AGGGATTTC	ACATCCTCCA	TCCCCAGCTC	CACAGCAGCC

TABLE 13-continued

Amino Terminal Nucleotide Sequence
(SEQ ID NO: 81)

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5001 ACAGTCCCAT TCATGGTGCC ATTCACCCTC AACTTCACCA TCACCAACCT
5051 GCAGTACGAG GAGGACATGC GGCACCCTGG TTCCAGGAAG TTCAACGCCA
5101 CAGAGAGAGA ACTGCAGGGT CTGCTCAAAC CCTTGTTTCAG GAATAGCAGT
5151 CTGGAATACC TCTATTCAGG CTGCAGACTA GCCTCACTCA GGCCAGAGAA
5201 GGATAGCTCA GCCATGGCAG TGGATGCCAT CTGCACACAT CGCCCTGACC
5251 CTGAAGACCT CGGACTGGAC AGAGAGCGAC TGTACTGGGA GCTGAGCAAT
5301 CTGACAAATG GCATCCAGGA GCTGGGCCCC TACACCCTGG ACCGGAACAG
5351 TCTCTATGTC AATGGTTTCA CCCATCGAAG CTCTATGCCC ACCACCAGCA
5401 CTCCTGGGAC CTCCACAGTG GATGTGGGAA CCTCAGGGAC TCCATCCTCC
5451 AGCCCCAGCC CCACG

TABLE 14

Amino Terminal Protein Sequence
(SEQ ID NO: 82)

5		1	ESVLEGTVTS	AYQVPSLSTR	LTRTDGIMEH	ITKIPNEAAH	RGTIRPVKGP
10		51	QTSTSPASPK	GLHTGGTKRM	ETTTTALKTT	TTALKTTSRA	TLTTSVYTPT
		101	LGTLTPLNAS	RQMASTILTE	MMITTPYVFP	DVPETTSSLA	TSLGAETSTA
		151	LPRTTPSVLN	RESETTASLV	SRSGAERSPV	IQTLDVSSSE	PDTTASWVIH
15							
		201	PAETIPTVSK	TTPNFFHSEL	DTVSSSTATSH	GADVSSAIPT	NISPSELDAL
		251	TPLVTISGTD	TSTTFPTLTK	SPHETETRRT	WLTHPAETSS	TIPRTIPNFS
20		301	HHESDATPSI	ATSPGAETSS	AIPIMTVSPG	AEDLVTSQVT	SSGTDNRNMTI
		351	PTLTLSPGEP	KTIASLVTHP	EAQTSSAIPT	STISPAVSRL	VTSMVTSLAA
		401	KTSTTNRALT	NSPGEPATTV	SLVTHPAQTS	PTVPWTTISIF	FHSKSDTTPS
25							
		451	MTTSHGAESS	SAVPTPTVST	EVPGVVTPLV	TSSRAVISTT	IPILTLSPGE
		501	PETTPSMATS	HGEEASSAIP	TPTVSPGVPG	VVTSLVTSR	AVTSTTIPIIL
30		551	TFSLGEPETT	PSMATSHGTE	AGSAVPTVLP	EVPGMVTSLV	ASSRAVTSTT
		601	LPTLTLSPGE	PETTPSMATS	HGAEASSTVP	TVSPEVPGVV	TSLVTSSSGV
		651	NSTSIPTLIL	SPGELETTPS	MATSHGAEAS	SAVPTPTVSP	GVSGVVTPLV
35							
		701	TSSRAVTSTT	IPILTLSSSE	PETTPSMATS	HGVEASSAVL	TVSPEVPGMV
		751	TSLVTSSRAV	TSTTIPTLTI	SSDEPETTTS	LVTHSEAKMI	SAIPTLAVSP
40		801	TVQGLVTSLV	TSSGSETSAF	SNLTVASSQP	ETIDSWVAHP	GTEASSVVPT
		851	LTVSTGEPFT	NISLVTHPAE	SSSTLPRTTS	RFSHSELDTM	PSTVTSPEAE
45		901	SSSAISTTIS	PGIPGVLTS	VTSSGRDISA	TFPTVPESPH	ESEATASWVT

TABLE 14-continued

Amino Terminal Protein Sequence
(SEQ ID NO: 82)

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951 HPAVTSTTVP RTTPNYSHSE PDTPPSIATS PGAEATSDFP TITVSPDVDP
1001 MVTSQVTSSG TDTSITIPTL TLSSGEPETT TSFITYSETH TSSAIPTLPV
1051 SPGASKMLTS LVISSGTDST TTFPTLTETP YEPETTAIQL IHPAETNTMV
1101 PRTTPKFSSS KSDTTLPVAI TSPGPEASSA VSTTTISPDM SDLVTSLVPS
1151 SGTDTSTTFP TLSETPYEPE TTATWLTHPA ETSTTVSGTI PNFSHRGSDT
1201 APSMVTSPGV DTRSGVPTTT IPPSIPGVVT SQVTSSATDT STAIPTLTPS
1251 PGEPETTASS ATHPGTQTGF TVPIRTVPSS EPDTMASWVT HPPQTSTPVS
1301 RTTSSFSHSS PDATPVMATS PRTEASSAVL TTISPGAPEM VTSQITSSGA
1351 ATSTTVPTLT HSPGMPETTA LLSTHPRTET SKTFPASTVF PQVSETTASL
1401 TIRPGAETST ALPTQTTSSL FTLLVTGTSR VDLSPITASPG VSAKTAPLST
1451 HPGTETSTMI PTSTLSLGLL ETTGLLATSS SAETSTSTLT LTVSPAVSGL
1501 SSASITTDKP QTVTSWNTET SPSVTSVGPP EFSRTVTGTT MTLIPSEMPT
1551 PPKTSHGEGV SPTTILRTTM VEATNLATTG SSPTVAKTTT TFNTLAGSLF
1601 TPLTTPGMST LASESVTSRT SYNHRSWIST TSSYNRRYWT PATSTPVTST
1651 FSPGISTSSI PSSTAATVPF MVPFTLNFTI TNLQYEEDMR HPGSRKFENAT
1701 ERELQGLLKP LFRNSSLEYL YSGCRLASLR PEKDSSAMAV DAICTHRPDP
1751 EDLGLDRERL YWELSNLTNG IQELGPYTLD RNSLYVNGFT HRSSMPTTST
1801 PGTSTVDVGT SGTPSSSPSP T

TABLE 15

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

(SEQ ID NO: 83)

1 GCCACAGTCC CATTTCATGGT GCCATTACCC CTCAACTTCA CCATCACCAA
51 CCTGCAGTAC GAGGAGGACA TGCGGCACCC TGGTTCCAGG AAGTTCAACG
101 CCACAGAGAG AGAACTGCAG GGTCTGCTCA AACCCCTGTT CAGGAATAGC
151 AGTCTGGAAT ACCTCTATTC AGGCTGCAGA CTAGCCTCAC TCAGGCCAGA
201 GAAGGATAGC TCAGCCATGG CAGTGGATGC CATCTGCATA CATCGCCCTG
251 ACCCTGAAGA CCTCGGACTG GACAGAGAGC GACTGTACTG GGAGCTGAGC
301 AATCTGACAA ATGGCATCCA GGAGCTGGGC CCCTACACCC TGGACCGGAA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCG AAGCTCTATG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGGATGTGG GAACCTCAGG GACTCCATCC
451 TCCAGCCCCA GCCCCACG

(SEQ ID NO: 84)

1 GCTGCTGGCC CTCTCCTGAT GCCGTTACCC CTCAACTTCA CCATCACCAA
51 CCTGCAGTAC GAGGAGGACA TGCCTCGCAC TGGCTCCAGG AAGTTCAACA
101 CCATGGAGAG TGTCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAACACC
151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA TTGACCTTGC TCAGGCCCAA
201 GAAAGATGGG GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGCCTTG
251 ACCCCAAAAG CCCTGGACTC AACAGGGAGC AGCTGTACTG GGAGCTAAGC
301 AACTGACCA ATGACATTGA AGAGCTGGGC CCCTACACCC TGGACAGGAA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GAGCTCTGTG TCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGGATCTCA GAACCTCAGG GACTCCATCC

TABLE 15- continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

5

451 TCCCTCTCCA GCCCCACAAT TATG

10 (SEQ ID NO: 85)

1 GCTGCTGGCC CTCTCCTGGT ACCATTACCC CTCAACTTCA CCATCACCAA

51 CCTGCAGTAT GGGGAGGACA TGGGTCACCC TGGCTCCAGG AAGTTCAACA

15

101 CCACAGAGAG GGTCTGCAG GGTCTGCTTG GTCCCATATT CAAGAACACC

151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTCTC TCAGGTCTGA

201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCATC CATCATCTTG

20

251 ACCCCAAAAG CCCTGGACTC AACAGAGAGC GGCTGTACTG GGAGCTGAGC

301 CAACTGACCA ATGGCATCAA AGAGCTGGGC CCCTACACCC TGGACAGGAA

25

351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GACCTCTGTG CCCACCACCA

401 GCACTCCTGG GACCTCCACA GTGGACCTTG GAACCTCAGG GACTCCATTC

451 TCCCTCCCAA GCCCCGCA

(SEQ ID NO: 86)

1 ACTGCTGGCC CTCTCCTGGT GCTGTTACCC CTCAACTTCA CCATCACCAA

51 CCTGAAGTAT GAGGAGGACA TGCATCGCCC TGGCTCCAGG AAGTTCAACA

35

101 CCACTGAGAG GGTCTGCAG ACTCTGCTTG GTCCTATGTT CAAGAACACC

151 AGTGTTGGCC TTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGTCCGA

40

201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGTCTTG

251 ACCCCAAAAG CCCTGGACTG GACAGAGAGC AGCTATACTG GGAGCTGAGC

301 CAGCTGACCA ATGGCATCAA AGAGCTGGGC CCCTACACCC TGGACAGGAA

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TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

5

351 CAGTCTCTAT GTCAATGGTT TCACCCATTG GATCCCTGTG CCCACCAGCA

10

401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGTCAGGGAC TCCATCCTCC

451 CTCCCCAGCC CCACA

(SEQ ID NO: 87)

15

1 GCTGCTGGCC CTCTCCTGGT GCCATTCACC CTCAACTTCA CCATCACCAA

51 CCTGCAGTAC GAGGAGGACA TGCATCACCC AGGCTCCAGG AAGTTCAACA

101 CCACGGAGCG GGTCCTGCAG GGTCTGCTTG GTCCCATGTT CAAGAACACC

20

151 AGTGTCGGCC TTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGTCCGA

201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGTCTTG

25

251 ACCCCAAAAG CCCTGGAGTG GACAGGGAGC AGCTATACTG GGAGCTGAGC

301 CAGCTGACCA ATGGCATCAA AGAGCTGGGT CCCTACACCC TGGACAGAAA

30

351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GACCTCTGCG CCCAACACCA

401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGACCTCAGG GACTCCATCC

451 TCCCTCCCCA GCCCTACA

35

(SEQ ID NO: 88)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA

51 CCTGCANTAN GNGGANNACA TGCNNCNCCC NGGNTCCAGG AAGTTCAACA

40

101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCCNTNTT CAAGAACACC

151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGTCCGA

201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGTCTTG

45

251 ACCCCAAAAG CCCTGGAGTG GACAGGGAGC AGCTATACTG GGAGCTGAGC

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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(SEQ ID NO: 89)

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(SEQ ID NO: 90)

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301 CAGCTGACCA ATGGCATCAA AGAGCTGGGT CCCTACACCC TGGACAGAAA

351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GACCTCTGCG CCCAACACCA

401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGACCTCAGG GACTCCATCC

451 TCCCTCCCCA GCCCTACA

1 TCTGCTGGCC CTCTCCTGGT GCCATTACCC CTCAACTTCA CCATCACCAA

51 CCTGCAGTAC GAGGAGGACA TGCATCACCC AGGCTCCAGG AAGTTCAACA

101 CCACGGAGCG GGTCTGCAG GGTCTGCTTG GTCCCATGTT CAAGAACACC

151 AGTGTCGGCC TTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCTGA

201 GAAGAATGGG GCAGCCACTG GAATGGATGC CATCTGCAGC CACCGTCTTG

251 ACCCCAAAAG CCCTGGACTC AACAGAGAGC AGCTGTACTG GGAGCTGAGC

301 CAGCTGACCC ATGGCATCAA AGAGCTGGGC CCCTACACCC TGGACAGGAA

351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GAGCTCTGTG GCCCCACCA

401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGACCTCAGG GACTCCATCC

451 TCCCTCCCCA GCCCCACA

1 ACAGCTGTTC CTCTCCTGGT GCCGTTACCC CTCAACTTTA CCATCACCAA

51 TCTGCAGTAT GGGGAGGACA TGCGTACCC TGGCTCCAGG AAGTTCAACA

101 CCACAGAGAG GGTCTGCAG GGTCTGCTTG GTCCCTTGTT CAAGAACTCC

151 AGTGTCGGCC CTCTGTACTC TGGCTGCAGA CTGATCTCTC TCAGGTCTGA

201 GAAGGATGGG GCAGCCACTG GAGTGGATGC CATCTGCACC CACCACCTTA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

251 ACCCTCAAAG CCCTGGACTG GACAGGGAGC AGCTGTACTG GCAGCTGAGC
301 CAGATGACCA ATGGCATCAA AGAGCTGGGC CCCTACACCC TGGACCGGAA
351 CAGTCTCTAC GTCAATGGTT TCACCCATCG GAGCTCTGGG CTCACCACCA
401 GCACTCCTTG GACTTCCACA GTTGACCTTG GAACCTCAGG GACTCCATCC
451 CCCGTCCCCA GCCCCACA

(SEQ ID NO: 91)

1 ACTGCTGGCC CTCTCCTGGT GCCATTCACC CTCAACTTCA CCATCACCAA
51 CCTGCAGTAT GAGGAGGACA TGCATCGCCC TGGATCTAGG AAGTTCAACA
101 CCACAGAGAG GGTCTGCAG GGTCTGCTTA GTCCCATTTT CAAGAACTCC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTCTC TCAGGCCCCGA
201 GAAGGATGGG GCAGCAACTG GAATGGATGC TGTCTGCCTC TACCACCCTA
251 ATCCCAAAAG ACCTGGACTG GACAGAGAGC AGCTGTACTG GGAGCTAAGC
301 CAGCTGACCC ACAACATCAC TGAGCTGGGC CCCTACAGCC TGGACAGGGA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GAACTCTGTG CCCACCACCA
401 GTACTCCTGG GACCTCCACA GTGTACTGGG CAACCACTGG GACTCCATCC
451 TCCTTCCCCG GCCACACA

(SEQ ID NO: 92)

1 GAGCCTGGCC CTCTCCTGAT ACCATTCACT TTCAACTTTA CCATCACCAA
51 CCTGCATTAT GAGGAAAACA TGCAACACCC TGGTTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAACACC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTCTC TCAGGCCCCGA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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201 GAAGGATGGG GCAGCAACTG GAATGGATGC TGTCTGCCTC TACCACCCTA
251 ATCCCAAAAG ACCTGGGCTG GACAGAGAGC AGCTGTACTG GGAGCTAAGC
301 CAGCTGACCC ACAACATCAC TGAGCTGGGC CCCTACAGCC TGGACAGGGA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GAACTCTGTG CCCACCACCA
401 GTACTCCTGG GACCTCCACA GTGTACTGGG CAACCACTGG GACTCCATCC
451 TCCTTCCCCG GCCACACA

(SEQ ID NO: 93)

1 GAGCCTGGCC CTCTCCTGAT ACCATTCACT TTCAACTTTA CCATCACCAA
51 CCTGCATTAT GAGGAAAACA TGCAACACCC TGGTTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTTCCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAACACC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA
201 GAAGCATGAG GCAGCCACTG GAGTGGACAC CATCTGTACC CACCGCGTTG
251 ATCCCATCGG ACCTGGACTG GACAGGGAGC GGCTATACTG GGAGCTGAGC
301 CAGCTGACCA ACAGCATTAC CGAACTGGGA CCCTACACCC TGGACAGGGA
351 CAGTCTCTAT GTCAATGGCT TCAACCCTCG GAGCTCTGTG CCAACCACCA
401 GCACTCCTGG GACCTCCACA GTGCACCTGG CAACCTCTGG GACTCCATCC
451 TCCCTGCCTG GCCACACA

(SEQ ID NO: 94)

1 GCCCCTGTCC CTCTCTTGAT ACCATTCACT CTCAACTTTA CCATCACCAA
51 CCTGCATTAT GAGGAAAACA TGCAACACCC TGGTTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTTCCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAACACC

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA
201 GAAGCATGAG GCAGCCACTG GAGTGGACAC CATCTGTACC CACCGCGTTG
251 ATCCCATCGG ACCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCCN GCCNCACA

(SEQ ID NO: 95)

1 TCTGCTGGCC CTCTCCTGGT GCCATTACCC CTCAACTTCA CCATCACCAA
51 CCTGCAGTAC GAGGAGGACA TGCATCACCC AGGCTCCAGG AAGTTCAACA
101 CCACGGAGCG GGTCCCTGCAG GGTCTGCTTG GTCCCATGTT CAAGAACACC
151 AGTGTCGGCC TTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCTGA
201 GAAGAATGGG GCAGCCACTG GAATGGATGC CATCTGCAGC CACCGTCTTG
251 ACCCCAAAAG CCCTGGACTC GACAGAGAGC AGCTGTACTG GGAGCTGAGC
301 CAGCTGACCC ATGGCATCAA AGAGCTGGGC CCCTACACCC TGGACAGGAA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GAGCTCTGTG GCCCCACCA
401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGACCTCAGG GACTCCATCC
451 TCCCTCCCCA GCCCCACA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

(SEQ ID NO: 96)

1 ACAGCTGTTC CTCTCCTGGT GCCGTTACCC CTCAACTTTA CCATCACCAA
51 TCTGCAGTAT GGGGAGGACA TGCCTCACCC TGGCTCCAGG AAGTTCAACA
101 CCACAGAGAG GGTCTGCAG GGTCTGCTTG GTCCCTTGTT CAAGAACTCC
151 AGTGTCGGCC CTCTGTACTC TGGCTGCAGA CTGATCTCTC TCAGGTCTGA
201 GAAGGATGGG GCAGCCACTG GAGTGGATGC CATCTGCACC CACCACCTTA
251 ACCCTCAAAG CCCTGGACTG GACAGGGAGC AGCTGTACTG GCAGCTGAGC
301 CAGATGACCA ATGGCATCAA AGAGCTGGGC CCCTACACCC TGGACCGGAA
351 CAGTCTCTAC GTCAATGGTT TCACCCATCG GAGCTCTGGG CTCACCACCA
401 GCACTCCTTG GACTTCCACA GTTGACCTTG GAACCTCAGG GACTCCATCC
451 CCCGTCCCCA GCCCCACA

(SEQ ID NO: 97)

1 ACTGCTGGCC CTCTCCTGGT GCCATTACCC CTAAACTTCA CCATCACCAA
51 CCTGCAGTAT GAGGAGGACA TGCATCGCCC TGGATCTAGG AAGTTCAACG
101 CCACAGAGAG GGTCTGCAG GGTCTGCTTA GTCCCATATT CAAGAACTCC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTCTC TCAGGCCCCGA
201 GAAGGATGGG GCAGCAACTG GAATGGATGC TGTCTGCCTC TACCACCCTA
251 ATCCCAAAG ACCTGGACTG GACAGAGAGC AGCTGTACTG GGAGCTAAGC
301 CAGCTGACCC ACAACATCAC TGAGCTGGGC CCCTACAGCC TGGACAGGGA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GAGCTCTATG ACGACCACCA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

401 GAACTCCTGA TACCTCCACA ATGCACCTGG CAACCTCGAG AACTCCAGCC

451 TCCCTGTCTG GACCTACG

(SEQ ID NO: 98)

1 ACCGCCAGCC CTCTCCTGGT GCTATTCACA ATCAACTGCA CCATCACCAA

51 CCTGCAGTAC GAGGAGGACA TGCCTCGCAC TGGCTCCAGG AAGTTCAACA

101 CCATGGAGAG TGTCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAACACC

151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA TTGACCTTGC TCAGGCCCAA

201 GAAAGATGGG GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGCCTTG

251 ACCCCAAAAG CCCTGGACTC AACAGGGAGC AGCTGTACTG GGAGCTAAGC

301 AAAGTGACCA ATGACATTGA AGAGCTGGGC CCCTACACCC TGGACAGGAA

351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GAGCTCTGTG TCCACCACCA

401 GCACTCCTGG GACCTCCACA GTGGATCTCA GAACCTCAGG GACTCCATCC

451 TCCCTCTCCA GCCCCACAAT TATG

(SEQ ID NO: 99)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA

51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA

101 CCACNGAGAG GGTCTACAG GGTCTGCTCA GGCCCTTGTT CAAGAACACC

151 AGTGTCAGCT CTCTGTACTC TGGTTGCAGA CTGACCTTGC TCAGGCCTGA

201 GAAGGATGGG GCAGCCACCA GAGTGGATGC TGCCTGCACC TACCGCCCTG

251 ATCCCAAAAG CCCTGGACTG GACAGAGAGC AACTATACTG GGAGCTGAGC

301 CAGCTAACCC ACAGCATCAC TGAGCTGGGA CCCTACACCC TGGACAGGGT

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru 145)

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351 CAGTCTCTAT GTCAATGGCT TCAACCCTCG GAGCTCTGTG CCAACCACCA
401 GCACTCCTGG GACCTCCACA GTGCACCTGG CAACCTCTGG GACTCCATCC
451 TCCCTGCCTG GCCACACA

(SEQ ID NO: 100)

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1 GCCCCTGTCC CTCTCTTGAT ACCATTACCC CTCAACTTTA CCATCACCAA
51 CCTGCATTAT GAAGAAAACA TGCAACACCC TGGTTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTTCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAGCACC
151 AGCGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA
201 GAAACATGGG GCAGCCACTG GAGTGGACGC CATCTGCACC CTCCGCCTTG
251 ATCCCACTGG TCCTGGACTG GACAGAGAGC GGCTATACTG GGAGCTGAGC
301 CAGCTGACCA ACAGCGTTAC AGAGCTGGGC CCCTACACCC TGGACAGGGA
351 CAGTCTCTAT GTCAATGGCT TCACCCAGCG GAGCTCTGTG CCAACCACCA
401 GTATTCCTGG GACCTCTGCA GTGCACCTGG AAACCTCTGG GACTCCAGCC
451 TCCCTCCCTG GCCACACA

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(SEQ ID NO: 101)

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1 GCCCCTGGCC CTCTCCTGGT GCCATTACCC CTCAACTTCA CTATCACCAA
51 CCTGCAGTAT GAGGTGGACA TGCCTCACCC TGGTTCCAGG AAGTTCAACA
101 CCACGGAGAG AGTCCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAGCACC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCTGA
201 AAAACGTGGG GCAGCCACCG GCGTGGACAC CATCTGCACT CACCGCCTTG
251 ACCCTCTAAA CCCTGGACTG GACAGAGAGC AGCTATACTG GGAGCTGAGC

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

301 AAACTGACCC GTGGCATCAT CGAGCTGGGC CCCTACCTCC TGGACAGAGG
351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GAACTTTGTG CCCATCACCA
401 GCACTCCTGG GACCTCCACA GTACACCTAG GAACCTCTGA AACTCCATCC
451 TCCCTACCTA GACCCATA

(SEQ ID NO: 102)

1 GTGCCTGGCC CTCTCCTGGT GCCATTACCC CTCAACTTCA CCATCACCAA
51 CTTGCAGTAT GAGGAGGCCA TGCACACCC TGGCTCCAGG AAGTTCAATA
101 CCACGGAGAG GGTCTACAG GGTCTGCTCA GGCCCTTGTT CAAGAATACC
151 AGTATCGGCC CTCTGTACTC CAGCTGCAGA CTGACCTTGC TCAGGCCAGA
201 GAAGGACAAG GCAGCCACCA GAGTGGATGC CATCTGTACC CACCACCCTG
251 ACCCTCAAAG CCCTGGACTG AACAGAGAGC AGCTGTACTG GGAGCTGAGC
301 CAGCTGACCC ACGGCATCAC TGAGCTGGGC CCCTACACCC TGGACAGGGA
351 CAGTCTCTAT GTCGATGGTT TCACTCATTG GAGCCCCATA CCGACCACCA
401 GCACTCCTGG GACCTCCATA GTGAACCTGG GAACCTCTGG GATCCCACCT
451 TCCCTCCCTG AAACCTACA

(SEQ ID NO: 103)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNNGANNACA TGCNNCNCCC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGAG GGTTCTGCAG GGTCTGCTCA AACCTTGTT CAGGAATAGC
151 AGTCTGGAAT ACCTCTATTC AGGCTGCAGA CTAGCCTCAC TCAGGCCAGA
201 GAAGGATAGC TCAGCCATGG CAGTGGATGC CATCTGCACA CATCGCCCTG

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru 145)

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251 ACCCTGAAGA CCTCGGACTG GACAGAGAGC GACTGTACTG GGAGCTGAGC
301 AATCTGACAA ATGGCATCCA GGAGCTGGGC CCCTACACCC TGGACCGGAA
351 CAGTCTCTAC GTCAATGGTT TCACCCATCG GAGCTCTGGG CTCACCACCA
401 GCACTCCTTG GACTTCCACA GTTGACCTTG GAACCTCAGG GACTCCATCC
451 CCCGTCCCCA GCCCCACA

(SEQ ID NO: 104)

1 ACTGCTGGCC CTCTCCTGGT GCCATTCACC CTCAACTTCA CCATCACCAA
51 CCTGCAGTAT GAGGAGGACA TGCATCGCCC TGGTTCCAGG AGGTTCAACA
101 CCACGGAGAG GGTCTGCAG GGTCTGCTCA CGCCCTTGTT CAAGAACACC
151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA
201 GAAGCAAGAG GCAGCCACTG GAGTGGACAC CATCTGTACC CACCGCGTTG
251 ATCCCATCGG ACCTGGACTG GACAGAGAGC GGCTATACTG GGAGCTGAGC
301 CAGCTGACCA ACAGCATCAC AGAGCTGGGA CCCTACACCC TGGATAGGGA
351 CAGTCTCTAT GTCAATGGCT TCAACCCTTG GAGCTCTGTG CCAACCACCA
401 GCACTCCTGG GACCTCCACA GTGCACCTGG CAACCTCTGG GACTCCATCC
451 TCCCTGCCTG GCCACACA

(SEQ ID NO: 105)

1 GCCCCTGTCC CTCTCTTGAT ACCATTCACC CTCAACTTTA CCATCACCGA
51 CCTGCATTAT GAAGAAAACA TGCAACACCC TGGTTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAGCACC
151 AGCGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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201 GAAACATGGG GCAGCCACTG GAGTGGACGC CATCTGCACC CTCCGCCTTG
251 ATCCCACTGG TCCTGGACTG GACAGAGAGC GGCTATACTG GGAGCTGAGC
301 CAGCTGACCA ACAGCGTTAC AGAGCTGGGC CCCTACACCC TGGACAGGGA
351 CAGTCTCTAT GTCAATGGCT TCACCCATCG GAGCTCTGTG CCAACCACCA
401 GTATTCCTGG GACCTCTGCA GTGCACCTGG AAACCTCTGG GACTCCAGCC
451 TCCCTCCCTG GCCACACA

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(SEQ ID NO: 106)

1 GCCCCTGGCC CTCTCCTGGT GCCATTACCC CTCAACTTCA CTATCACCAA
51 CCTGCAGTAT GAGGAGGACA TCGTACACCC TGGTTCCAGG AAGTTCAGCA
101 CCACGGAGAG AGTCCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAACACC
151 AGTGTGAGCT CTCTGTACTC TGGTTGCAGA CTGACCTTGC TCAGGCCTGA
201 GAAGGATGGG GCAGCCACCA GAGTGGATGC TGTCTGCACC CATCGTCCTG
251 ACCCCAAAAG CCCTGGACTG GACAGAGAGC GGCTGTACTG GAAGCTGAGC
301 CAGCTGACCC ACGGCATCAC TGAGCTGGGC CCCTACACCC TGGACAGGCA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GAGCTCTATG ACGACCACCA
401 GAACTCCTGA TACCTCCACA ATGCACCTGG CAACCTCGAG AACTCCAGCC
451 TCCCTGTCTG GACCTACG

(SEQ ID NO: 107)

1 ACCGCCAGCC CTCTCCTGGT GCTATTCACA ATTAAGTTCA CCATCACTAA
51 CCTGCGGTAT GAGGAGAACA TGCATCACCC TGGCTCTAGA AAGTTTAACA
101 CCACGGAGAG AGTCCTTCAG GGTCTGCTCA GGCCTGTGTT CAAGAACACC

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACCACGC TCAGGCCCAA
201 GAAGGATGGG GCAGCCACCA AAGTGGATGC CATCTGCACC TACCGCCCTG
251 ATCCCAAAAG CCCTGGACTG GACAGAGAGC AGCTATACTG GGAGCTGAGC
301 CAGCTAACCC ACAGCATCAC TGAGCTGGGC CCCTACACCC AGGACAGGGA
351 CAGTCTCTAT GTCAATGGCT TCACCCATCG GAGCTCTGTG CCAACCACCA
401 GTATTCCTGG GACCTCTGCA GTGCACCTGG AACCTCTGG GACTCCAGCC
451 TCCCTCCCTG GCCACACA

(SEQ ID NO: 108)

1 GCCCCTGGCC CTCTCCTGGT GCCATTCACC CTCAACTTCA CTATCACCAA
51 CCTGCAGTAT GAGGAGGACA TCGTCACCC TGGTTCCAGG AAGTTCAACA
101 CCACGGAGAG AGTCCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAGCACC
151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCTGA
201 AAAACGTGGG GCAGCCACCG GCGTGGACAC CATCTGCACT CACCGCCTTG
251 ACCCTCTAAA CCCAGGACTG GACAGAGAGC AGCTATACTG GGAGCTGAGC
301 AAAC TGACCC GTGGCATCAT CGAGCTGGGC CCCTACCTCC TGGACAGAGG
351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GACCTCTGTG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGGACCTTG GAACCTCAGG GACTCCATTC
451 TCCCTCCCAA GCCCCGCA

(SEQ ID NO: 109)

1 NCNNTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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101 CCACNGAGAG GGCCTGCAG ACTCTGCTTG GTCCTATGTT CAAGAACACC
151 AGTGTTGGCC TTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGTCCGA
201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGTCTTG
251 ACCCCAAAAG CCCTGGAGTG GACAGGGAGC AACTATACTG GGAGCTGAGC
301 CAGCTGACCA ATGGCATTAA AGAACTGGGC CCCTACACCC TGGACAGGAA
351 CAGTCTCTAT GTCAATGGGT TCACCCATTG GATCCCTGTG CCCACCAGCA
401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGTGAGGGAC TCCATCCTCC
451 CTCCCCAGCC CCACA

(SEQ ID NO: 110)

1 ACTGCTGGCC CTCTCCTGGT GCCGTTACCC CTCAACTTCA CCATCACCAA
51 CCTGAAGTAC GAGGAGGACA TGCATTGCCC TGGCTCCAGG AAGTTCAACA
101 CCACAGAGAG AGTCCTGCAG AGTCTGCTTG GTCCCATGTT CAAGAACACC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGTCCGA
201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGTCTTG
251 ACCCCAAAAG CCCTGGAGTG GACAGGGAGC AGCTATACTG GGAGCTGAGC
301 CAGCTGACCA ATGGCATCAA AGAGCTGGGT CCCTACACCC TGGACAGAAA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GACCTCTGCG CCCAACACCA
401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGACCTCAGG GACTCCATCC
451 TCCCTCCCCA GCCCTACA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

(SEQ ID NO: 111)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCCNTNTT CAAGAACNCC
151 AGTGTNGGCC NTCTGTACTC TGGCTGCAGA CTGACCTNNC TCAGGNCNGA
201 GAAGNATGGN GCAGCCACTG GANTGGATGC CATCTGCANC CACCNNCNTN
251 ANCCCCAAAAG NCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATTG GATCCCTGTG CCCACCAGCA
401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGTCAGGGAC TCCATCCTCC
451 CTCCCCAGCC CCACA

(SEQ ID NO: 112)

1 ACTGCTGGCC CTCTCCTGGT GCCGTTTACC CTCAACTTCA CCATCACCAA
51 CCTGAAGTAC GAGGAGGACA TGCATTGCCC TGGCTCCAGG AAGTTCAACA
101 CCACAGAGAG AGTCCTGCAG AGTCTGCTTG GTCCCATGTT CAAGAACACC
151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACCTCGC TCAGGTCCGA
201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGTGTTG
251 ACCCCAAAAG CCCTGGAGTG GACAGGGAGC AGCTATACTG GGAGCTGAGC
301 CAGCTGACCA ATGGCATCAA AGAGCTGGGT CCCTACACCC TGGACAGAAA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GACCTCTGCG CCCAACACCA
401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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451 TCCNTCCCCN GCCNCACA

10 (SEQ ID NO: 113)

1 TCTGCTGGCC CTCTCCTGGT GCCATTACCC CTCAACTTCA CCATCACCAA

51 CCTGCAGTAC GAGGAGGACA TGCATCACCC AGGCTCCAGG AAGTTCAACA

15

101 CCACGGAGCG GGTCCTGCAG GGTCTGCTTG GTCCCATGTT CAAGAACACC

151 AGTGTGCGCC TTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCTGA

201 GAAGAATGGG GCAACCACTG GAATGGATGC CATCTGCACC CACCGTCTTG

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251 ACCCCAAAAG CCCTGGACTG NACAGNGAGC NGCTNCTACTG GGAGCTNAGC

301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA

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351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA

401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC

451 TCCNTCCCCN GCCNCACA

30 (SEQ ID NO: 114)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA

51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA

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101 CCACNGAGAG GGTCTCTGCAG GGTCTGCTCA AACCTTGTT CAGGAATAGC

151 AGTCTGGAAT ACCTCTATTC AGGCTGCAGA CTAGCCTCAC TCAGGCCAGA

40

201 GAAGGATAGC TCAGCCATGG CAGTGGATGC CATCTGCACA CATCGCCCTG

251 ACCCTGAAGA CCTCGGACTG GACAGAGAGC GACTGTACTG GGAGCTGAGC

301 AATCTGACAA ATGGCATCCA GGAGCTGGGC CCCTACACCC TGGACCGGAA

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351 CAGTCTCTAT GTCAATGGTT TCACCCATCG AAGCTCTATG CCCACCACCA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

401 GCACTCCTGG GACCTCCACA GTGGATGTGG GAACCTCAGG GACTCCATCC

451 TCCAGCCCCA GCCCCACG

(SEQ ID NO: 115)

1 ACTGCTGGCC CTCTCCTGAT ACCATTACCC CTCAACTTCA CCATCACCAA

51 CCTGCAGTAT GGGGAGGACA TGGGTCACCC TGGCTCCAGG AAGTTCAACA

101 CCACAGAGAG GGTCTGCAG GGTCTGCTTG GTCCCATATT CAAGAACACC

151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTCTC TCAGGTCTGA

201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCATC CATCATCTTG

251 ACCCCAAAAG CCCTGGACTC AACAGAGAGC GGCTGTACTG GGAGCTGAGC

301 CAACTGACCA ATGGCATCAA AGAGCTGGGC CCCTACACCC TGGACAGGAA

351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GACCTCTGTG CCCACCACCA

401 GCACTCCTGG GACCTCCACA GTGGACCTTG GAACCTCAGG GACTCCATTC

451 TCCCTCCCAA GCCCCGCA

(SEQ ID NO: 116)

1 ACTGCTGGCC CTCTCCTGGT GCTGTTACCC CTCAACTTCA CCATCACCAA

51 CCTGAAGTAT GAGGAGGACA TGCATCGCCC TGGCTCCAGG AAGTTCAACA

101 CCACTGAGAG GGTCTGCAG ACTCTGCTTG GTCCTATGTT CAAGAACACC

151 AGTGTTGGCC TTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGTCCGA

201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGTCTTG

251 ACCCCAAAAG CCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCH GANCTCTGNG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCCN GCCNCACA

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(SEQ ID NO: 117)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGAG AGTCCTTCAG GGTCTGCTCA GGCCTGTGTT CAAGAACACC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCCAA
201 GAAGGATGGG GCAGCCACCA AAGTGGATGC CATCTGCACC TACCGCCCTG
251 ATCCCAAAAG CCCTGGACTG GACAGAGAGC AGCTATACTG GGAGCTGAGC
301 CAGCTAACCC ACAGCATCAC TGAGCTGGGC CCCTACACCC AGGACAGGGA
351 CAGTCTCTAT GTCAATGGCT TCACCCATCG GAGCTCTGTG CCAACCACCA
401 GTATTCCTGG GACCTCTGCA GTGCACCTGG AAACCACTGG GACTCCATCC
451 TCCTTCCCCG GCCACACA

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(SEQ ID NO: 118)

1 GAGCCTGGCC CTCTCCTGAT ACCATTCACT TTCAACTTTA CCATCACCAA
51 CCTGCGTTAT GAGGAAAACA TGCAACACCC TGGTTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTCTGCAG GGTCTGCTCA CGCCCTTGTT CAAGAACACC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA
201 GAAGCAGGAG GCAGCCACTG GAGTGGACAC CATCTGTACC CACCGCGTTG

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TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru 145)

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251 ATCCCATCGG ACCTGGACTG GACAGAGAGC GGCTATACTG GGAGCTGAGC
301 CAGCTGACCA ACAGCATCAC AGAGCTGGGA CCCTACACCC TGGATAGGGA
351 CAGTCTCTAT GTCGATGGCT TCAACCCTTG GAGCTCTGTG CCAACCACCA
401 GCACTCCTGG GACCTCCACA GTGCACCTGG CAACCTCTGG GACTCCATCC
451 CCCCTGCCTG GCCACACA

(SEQ ID NO: 119)

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1 GCCCCTGTCC CTCTCTTGAT ACCATTACCC CTCAACTTTA CCATCACCGA
51 CCTGCATTAT GAAGAAAACA TGCAACACCC TGGTTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTTCCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAGCACC
151 AGCGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA
201 GAAACATGGG GCAGCCACTG GAGTGGACGC CATCTGCACC CTCCGCCTTG
251 ATCCCACTGG TCCTGGACTG GACAGAGAGC GGCTATACTG GGAGCTGAGC
301 CAGCTGACCA ACAGCATCAC AGAGCTGGGA CCCTACACCC TGGATAGGGA
351 CAGTCTCTAT GTCAATGGCT TCAACCCTTG GAGCTCTGTG CCAACCACCA
401 GCACTCCTGG GACCTCCACA GTGCACCTGG CAACCTCTGG GACTCCATCC
451 TCCCTGCCTG GCCACACA

(SEQ ID NO: 120)

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1 ACTGCTGGCC CTCTCCTGGT GCCGTTACCC CTCAACTTCA CCATCACCAA
51 CCTGAAGTAC GAGGAGGACA TGCATTGCCC TGGCTCCAGG AAGTTCAACA
101 CCACAGAGAG AGTCCTGCAG AGTCTGCATG GTCCCATGTT CAAGAACACC
151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGTCCGA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCACC CACCGTCTTG
10 251 ACCCCAAAAG CCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA
15 401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCCN GCCNCACA

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(SEQ ID NO: 121)

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TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCTGA
201 AAAACGTGGG GCAGCCACCG GCGTGGACAC CATCTGCACT CACCGCCTTG
251 ACCCTCTAAA CCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCH GANCTCTGNG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCCN GCCNCACA

(SEQ ID NO: 123)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCCC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCCNTNTT CAAGAACNCC
151 AGTGTNGGCC NTCTGTACTC TGGCTGCAGA CTGACCTNNC TCAGGNCNGA
201 GAAGNATGGN GCAGCCACTG GANTGGATGC CATCTGCANC CACCNNCNTN
251 ANCCCAAAAG NCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TTCACCCTCG GAGCTCTGTG CCAACCACCA
401 GCACTCCTGG GACCTCCACA GTGCACCTGG CAACCTCTGG GACTCCATCC
451 TCCCTGCCTG GCCACACA

(SEQ ID NO: 124)

45
1 GCCCTGTCC CTCTCTTGAT ACCATTACCC CTCAACTTTA CCATCACCAA
51 CCTGCATTAT GAAGAAAACA TGCAACACCC TGGTTCCAGG AAGTTCAACA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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101 CCACGGAGCG GGTCTGCAG GGTCTGCTTG GTCCCATGTT CAAGAACACA
151 AGTGTGCGGCC TTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCTGA
201 GAAGAAATGGG GCAGCCACTG GAATGGATGC CATCTGCAGC CACCGTCTTG
251 ACCCCAAAAG CCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCCN GCCNCACA

(SEQ ID NO: 125)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCCC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCCNTNTT CAAGAACNCC
151 AGTGTNGGCC NTCTGTACTC TGGCTGCAGA CTGACCTNNC TCAGGNCNGA
201 GAAGNATGGN GCAGCCACTG GANTGGATGC CATCTGCANC CACCNNCNTN
251 ANCCCAAAAG NCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GAACTCTGTG CCCACCACCA
401 GTACTCCTGG GACCTCCACA GTGTACTGGG CAACCACTGG GACTCCATCC
451 TCCTTCCCCG GCCACACA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

(SEQ ID NO: 126)

1 GAGCCTGGCC CTCTCCTGAT ACCATTCACT TTCAACTTTA CCATCACCAA
51 CCTGCATTAT GAGGAAAACA TGCAACACCC TGGTTCAGG AAGTTCAACA
101 CCACGGAGAG GGTTCCTGCAG GGTCTGCTCA CGCCCTTGTT CAAGAACACC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA
201 GAAGCAGGAG GCAGCCACTG GAGTGGACAC CATCTGTACC CACCGCGTTG
251 ATCCCATCGG ACCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCN GCCNCACA

(SEQ ID NO: 127)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCNCC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCCNTNTT CAAGAACNCC
151 AGTGTTGGCC NTCTGTACTC TGGCTGCAGA CTGACCTNNC TCAGGNCNGA
201 GAAGNATGGN GCAGCCACTG GANTGGATGC CATCTGCANC CACCNNCNTN
251 ANCCCAAAG NCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GAGCTCTGTG CCAACCACCA
401 GCAGTCCTGG GACCTCCACA GTGCACCTGG CAACCTCTGG GACTCCATCC

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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451 TCCCTGCCTG GCCACACA

10 (SEQ ID NO: 128)

1 GCCCCTGTCC CTCTCTTGAT ACCATTACCC CTCAACTTTA CCATCACCAA

51 CCTGCATTAT GAAGAAAACA TGCAACACCC TGGTTCAGG AAGTTCAACA

15

101 CCACGGAGAG GGTTCCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAGCACC

151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA

201 GAAACATGGG GCAGCCACTG GAGTGGACGC CATCTGCACC CTCCGCCTTG

20

251 ATCCCACTGG TCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC

301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA

351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA

401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC

451 TCCNTCCCN GCCNCACA

30 (SEQ ID NO: 129)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA

51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA

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101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCNTNTT CAAGAACNCC

151 AGTGTTGGCC NTCTGTACTC TGGCTGCAGA CTGACCTNNC TCAGGNCNGA

40

201 GAAGNATGGN GCAGCCACTG GANTGGATGC CATCTGCANC CACCNNCNTN

251 ANCCCAAAAG NCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC

301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA

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351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GACCTCTGTG CCCACCACCA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

5 401 GCACTCCTGG GACCTCCACA GTGCACCTGG CAACCTCTGG GACTCCATCC

10 451 TCCCTGCCTG GCCACACA

(SEQ ID NO: 130)

1 GCCCCTGTCC CTCTCTTGAT ACCATTACCC CTCAACTTTA CCATCACCAA

15 51 CCTGCAGTAT GAGGAGGACA TGCATCGCCC TGGATCTAGG AAGTTCAACA

101 CCACAGAGAG GGTCTGCAG GGTCTGCTTA GTCCCATTTT CAAGAACTCC

151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTCTC TCAGGCCCGA

20 201 GAAGGATGGG GCAGCAACTG GAATGGATGC TGTCTGCCTC TACCACCCTA

251 ATCCCAAAAG ACCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC

301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA

351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA

401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC

451 TCCNTCCCCN GCCNCACA

(SEQ ID NO: 131)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA

35 51 CCTGCANTAN GNGGANNACA TGCNNCNCNCC NGGNTCCAGG AAGTTCAACA

101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCCNNTTT CAAGAACNCC

40 151 AGTGTTGGCC NTCTGTACTC TGGCTGCAGA CTGACCTNNC TCAGGNCNGA

201 GAAGNATGGN GCAGCCACTG GANTGGATGC CATCTGCANC CACCNNCNTN

251 ANCCCAAAAG NCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC

45 301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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351 CAGTCTCTAT GTCAATGGTT TCACCCATTG GAGCTCTGGG CTCACCACCA
10 401 GCACTCCTTG GACTTCCACA GTTGACCTTG GAACCTCAGG GACTCCATCC
451 CCCGTCCCCA GCCCCACA

(SEQ ID NO: 132)

15

1 ACTGCTGGCC CTCTCCTGGT GCCATTACCC CTAAACTTCA CCATCACCAA
51 CCTGCAGTAT GAGGAGGACA TGCATCGCCC TGGATCTAGG AAGTTCAACG
101 CCACAGAGAG GGTCTGCAG GGTCTGCTTA GTCCCATATT CAAGAACACC
20 151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGACCTGA
201 GAAGCAGGAG GCAGCCACTG GAGTGGACAC CATCTGTACC CACCGCGTTG
25 251 ATCCCATCGG ACCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA
30 401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCCN GCCNCACA

(SEQ ID NO: 133)

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1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCCNNTTT CAAGAACNCC
40 151 AGTGTNGGCC NTCTGTACTC TGGCTGCAGA CTGACCTNNC TCAGGNCNGA
201 GAAGNATGGN GCAGCCACTG GANTGGATGC CATCTGCANC CACCNNCNTN
45 251 ANCCCAAAG NCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GAGCTTTGGG CTCACCACCA
401 GCACTCCTTG GACTTCCACA GTTGACCTTG GAACCTCAGG GACTCCATCC
451 CCCGTCCCCA GCCCCACA

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(SEQ ID NO: 134)

1 ACTGCTGGCC CTCTCCTGGT GCCATTACCC CTAAACTTCA CCATCACCAA
51 CCTGCAGTAT GAGGAGGACA TGCATCGCCC TGGCTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTCTTCAG GGTCTGCTTA CGCCCTTGTT CAGGAACACC
151 AGTGTGAGCT CTCTGTACTC TGGTTGCAGA CTGACCTTGC TCAGGCCTGA
201 GAAGGATGGG GCAGCCACCA GAGTGGATGC TGTCTGCACC CATCGTCCTG
251 ACCCCAAAAG CCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCCN GCCNCACA

(SEQ ID NO: 135)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCNTNTT CAAGAACNCC
151 AGTGTNGGCC NTCTGTACTC TGGCTGCAGA CTGACCTNNC TCAGGNCNGA
201 GAAGNATGGN GCAGCCACTG GANTGGATGC CATCTGCANC CACCNNCNTN

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

251 ANCCCAAAAG NCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATTG GATCCCTGTG CCCACCAGCA
401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGTCAGGGAC TCCATCCTCC
451 CTCCCCAGCC CCACA

(SEQ ID NO: 136)

1 ACTGCTGGCC CTCTCCTGGT ACCATTCACC CTCAACTTCA CCATCACCAA
51 CCTGCAGTAT GGGGAGGACA TGGGTCACCC TGGCTCCAGG AAGTTCAACA
101 CCACAGAGAG GGTCTGCAG GGTCTGCTTG GTCCCATATT CAAGAACACC
151 AGTGTTGGCC CTCTGTACTC TGGCTGCAGA CTGACCTCTC TCAGGTCCGA
201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCATC CATCATCTTG
251 ACCCAAAAAG CCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCN GCCNCACA

(SEQ ID NO: 137)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGNG NGTNCTGCAG GGTCTGCTNN NNCCCNNTTT CAAGAACNCC
151 AGTGTTGGCC NTCTGTACTC TGGCTGCAGA CTGACCTNNC TCAGGNCNGA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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201 GAAGNATGGN GCAGCCACTG GANTGGATGC CATCTGCANC CACCNNCNTN
251 ANCCCAAAAG NCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GACCTTTGCG CCCAACACCA
401 GCACTCCTGG GACCTCCACA GTGGACCTTG GGACCTCAGG GACTCCATCC
451 TCCCTCCCC AGCCCTACA

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(SEQ ID NO: 138)

1 TCTGCTGGCC CTCTCCTGGT GCCATTCACC CTCAACTTCA CCATCACCAA
51 CCTGCAGTAC GAGGAGGACA TGCATCACCC AGGCTCCAGG AAGTTCAACA
101 CCACGGAGCG GGTCTGCAG GGTCTGCTTG GTCCCATGTT CAAGAACACC
151 AGTGTGCGCC TTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCTGA
201 GAAGAATGGG GCAGCCACCA GAGTGGATGC TGTCTGCACC CATCGTCCTG
251 ACCCAAAAAG CCCTGGACTG NACAGNGAGC NGCTNTACTG GGAGCTNAGC
301 CANCTGACCA ANNNCATCNN NGAGCTGGGN CCCTACACCC TGGACAGGNA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCN GANCTCTGNG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGNACNTNG GNACCTCNGG GACTCCATCC
451 TCCNTCCCCN GCCNCACA

(SEQ ID NO: 139)

1 NCNNCTGNCC CTCTCCTGNT NCCNTTCACC NTCAACTTNA CCATCACCAA
51 CCTGCANTAN GNGGANNACA TGCNNCNCNC NGGNTCCAGG AAGTTCAACA
101 CCACNGAGAG GGTCTGCAG GGTCTGCTCA AGCCCTTGTT CAAGAGCACC

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

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151 AGTGTTGGCC CTCTGTATTC TGGCTGCAGA CTGACCTTGC TCAGGCCTGA
201 GAAGGACGGA GTAGCCACCA GAGTGGACGC CATCTGCACC CACCGCCCTG
251 ACCCCAAAAT CCCTGGGCTA GACAGACAGC AGCTATACTG GGAGCTGAGC
301 CAGCTGACCC ACAGCATCAC TGAGCTGGGA CCCTACACCC TGGATAGGGA
351 CAGTCTCTAT GTCAATGGTT TCACCCAGCG GAGCTCTGTG CCCACCACCA
401 GCACTCCTGG GACTTTCACA GTACAGCCGG AACCTCTGA GACTCCATCA
451 TCCCTCCCTG GCCCCACA

(SEQ ID NO: 140)

1 GCCACTGGCC CTGTCCTGCT GCCATTCACC CTCAATTTTA CCATCACTAA
51 CCTGCAGTAT GAGGAGGACA TGCATCGCCC TGGCTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTCTTCAG GGTCTGCTTA TGCCCTTGTT CAAGAACACC
151 AGTGTCAGCT CTCTGTACTC TGGTTGCAGA CTGACCTTGC TCAGGCCTGA
201 GAAGGATGGG GCAGCCACCA GAGTGGATGC TGTCTGCACC CATCGTCCTG
251 ACCCCAAAAG CCCTGGACTG GACAGAGAGC GGCTGTACTG GAAGCTGAGC
301 CAGCTGACCC ACGGCATCAC TGAGCTGGGC CCCTACACCC TGGACAGGCA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCA GAGCTCTATG ACGACCACCA
401 GAACTCCTGA TACCTCCACA ATGCACCTGG CAACCTCGAG AACTCCAGCC
451 TCCCTGTCTG GACCTACG

(SEQ ID NO: 141)

1 ACCGCCAGCC CTCTCCTGGT GCTATTCACA ATTAATTCA CCATCACTAA
51 CCTGCGGTAT GAGGAGAACA TGCATCACCC TGGCTCTAGA AAGTTTAACA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

101 CCACGGAGAG AGTCCTTCAG GGTCTGCTCA GGCCTGTGTT CAAGAACACC
151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACCTTGC TCAGGCCCAA
201 GAAGGATGGG GCAGCCACCA AAGTGGATGC CATCTGCACC TACCGCCCTG
251 ATCCCAAAG CCCTGGACTG GACAGAGAGC AGCTATACTG GGAGCTGAGC
301 CAGCTAACCC ACAGCATCAC TGAGCTGGGC CCCTACACCC TGGACAGGGA
351 CAGTCTCTAT GTCAATGGTT TCACACAGCG GAGCTCTGTG CCCACCACTA
401 GCATTCCTGG GACCCCCACA GTGGACCTGG GAACATCTGG GACTCCAGTT
451 TCTAACCTG GTCCCTCG

(SEQ ID NO: 142)

1 GCTGCCAGCC CTCTCCTGGT GCTATTCCT CTCAACTTCA CCATCACCAA
51 CCTGCGGTAT GAGGAGAACA TGCAGCACCC TGGCTCCAGG AAGTTCAACA
101 CCACGGAGAG GGTCTTCAG GGCCTGCTCA GGTCCCTGTT CAAGAGCACC
151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACTTTGC TCAGGCCTGA
201 AAAGGATGGG ACAGCCACTG GAGTGGATGC CATCTGCACC CACCACCCTG
251 ACCCAAAG CCCTAGGCTG GACAGAGAGC AGCTGTATTG GGAGCTGAGC
301 CAGCTGACCC ACAATATCAC TGAGCTGGGC CACTATGCCC TGGACAACGA
351 CAGCCTCTTT GTCAATGGTT TCACTCATCG GAGCTCTGTG TCCACCACCA
401 GCACTCCTGG GACCCCCACA GTGTATCTGG GAGCATCTAA GACTCCAGCC
451 TCGATATTG GCCCTTCA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

(SEQ ID NO: 143)

1 GCTGCCAGCC ATCTCCTGAT ACTATTCACC CTCAACTTCA CCATCACTAA
51 CCTGCGGTAT GAGGAGAACA TGTGGCCTGG CTCCAGGAAG TTCAACACTA
101 CAGAGAGGGT CCTTCAGGGC CTGCTAAGGC CCTTGTTCAA GAACACCAGT
151 GTTGGCCCTC TGTACTCTGG CTCCAGGCTG ACCTTGCTCA GGCCAGAGAA
201 AGATGGGGAA GCCACCGGAG TGGATGCCAT CTGCACCCAC CGCCCTGACC
251 CCACAGGCCC TGGGCTGGAC AGAGAGCAGC TGTATTTGGA GCTGAGCCAG
301 CTGACCCACA GCATCACTGA GCTGGGCCCC TACACACTGG ACAGGGACAG
351 TCTCTATGTC AATGGTTTCA CCCATCGGAG CTCTGTACCC ACCACCAGC

(SEQ ID NO: 144)

1 ACCGGGGTGG TCAGCGAGGA GCCATTCACA CTGAACTTCA CCATCAACAA
51 CCTGCGCTAC ATGGCGGACA TGGGCCAACC CGGCTCCCTC AAGTTCAACA
101 TCACAGACAA CGTCATGAAG CACCTGCTCA GTCCTTTGTT CCAGAGGAGC
151 AGCCTGGGTG CACGGTACAC AGGCTGCAGG GTCATCGCAC TAAGGTCTGT
201 GAAGAACGGT GCTGAGACAC GGGTGGACCT CCTCTGCACC TACCTGCAGC
251 CCCTCAGCGG CCCAGGTCTG CCTATCAAGC AGGTGTTCCA TGAGCTGAGC
301 CAGCAGACCC ATGGCATCAC CCGGCTGGGC CCCTACTCTC TGGACAAAGA
351 CAGCCTCTAC CTTAACGGTT ACAATGAACC TGGTCTAGAT GAGCCTCCTA
401 CAACTCCCAA GCCAGCCACC ACATTCCTGC CTCCTCTGTC AGAAGCCACA
451 ACA

TABLE 15-continued

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 83 thru SEQ ID NO: 145)

(SEQ ID NO: 145)

1 GCCATGGGGT ACCACCTGAA GACCCTCACA CTCAACTTCA CCATCTCCAA
51 TCTCCAGTAT TCACCAGATA TGGGCAAGGG CTCAGCTACA TTCAACTCCA
101 CCGAGGGGGT CCTTCAGCAC CTGCTCAGAC CCTTGTTCCA GAAGAGCAGC
151 ATGGGCCCCCT TCTACTTGGG TTGCCAACTG ATCTCCCTCA GGCCTGAGAA
201 GGATGGGGCA GCCACTGGTG TGGACACCAC CTGCACCTAC CACCCTGACC
251 CTGTGGGCCC CGGGCTGGAC ATACAGCAGC TTTACTGGGA GCTGAGTCAG
301 CTGACCCATG GTGTCACCCA ACTGGGCTTC TATGTCCTGG ACAGGGATAG
351 CCTCTTCATC AATGGCTATG CACCCAGAA TTTATCAATC CGGGGCGAGT
401 ACCAGATAAA TTTCCACATT GTCAACTGGA ACCTCAGTAA TCCAGACCCC
451 ACATCCTCAG AGTAC

TABLE 17

Carboxy Terminal Nucleotide Sequence
(SEQ ID NO: 147)

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1 GCCATGGGGT ACCACCTGAA GACCCTCACA CTCAACTTCA CCATCTCCAA
51 TCTCCAGTAT TCACCAGATA TGGGCAAGGG CTCAGCTACA TTCAACTCCA
101 CCGAGGGGGT CCTTCAGCAC CTGCTCAGAC CCTTGTTCCA GAAGAGCAGC
151 ATGGGCCCCT TCTACTTGGG TTGCCAACTG ATCTCCCTCA GGCCTGAGAA
201 GGATGGGGCA GCCACTGGTG TGGACACCAC CTGCACCTAC CACCCTGACC
251 CTGTGGGCCC CGGGCTGGAC ATACAGCAGC TTTACTGGGA GCTGAGTCAG
301 CTGACCCATG GTGTCACCCA ACTGGGCTTC TATGTCCTGG ACAGGGATAG
351 CCTCTTCATC AATGGCTATG CACCCCAGAA TTTATCAATC CGGGGCGAGT
401 ACCAGATAAA TTTCCACATT GTCAACTGGA ACCTCAGTAA TCCAGACCCC
451 ACATCCTCAG AGTACATCAC CCTGCTGAGG GACATCCAGG ACAAGGTCAC
501 CACACTCTAC AAAGGCAGTC AACTACATGA CACATTCCGC TTCTGCCTGG
551 TCACCAACTT GACGATGGAC TCCGTGTTGG TCACTGTCAA GGCATTGTTC
601 TCCTCCAATT TGGACCCCAG CCTGGTGGAG CAAGTCTTTC TAGATAAGAC
651 CCTGAATGCC TCATTCCATT GGCTGGGCTC CACCTACCAG TTGGTGGACA
701 TCCATGTGAC AGAAATGGAG TCATCAGTTT ATCAACCAAC AAGCAGCTCC
751 AGCACCCAGC ACTTCTACCT GAATTTACC ATCACCAACC TACCATATTC
801 CCAGGACAAA GCCCAGCCAG GCACCACCAA TTACCAGAGG AACAAAAGGA
851 ATATTGAGGA TGCGCTCAAC CAACTCTTCC GAAACAGCAG CATCAAGAGT
901 TATTTTCTG ACTGTCAAGT TTCAACATTC AGGTCTGTCC CCAACAGGCA

TABLE 17-continued

Carboxy Terminal Nucleotide Sequence
(SEQ ID NO: 147)

5
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951 CCACACCGGG GTGGACTCCC TGTGTAACCT CTCGCCACTG GCTCGGAGAG *
1001 TAGACAGAGT TGCCATCTAT GAGGAATTTC TCGGATGAC CCGGAATGGT
1051 ACCCAGCTGC AGAACTTCAC CCTGGACAGG AGCAGTGTCC TTGTGGATGG
1101 GTATTCTCCC AACAGAAATG AGCCCTTAAC TGGGAATTCT GACCTTCCCT
1151 TCTGGGCTGT CATCCTCATC GGCTTGGCAG GACTCCTGGG ACTCATCACA
1201 TGCCTGATCT GCGGTGTCCT GGTGACCACC CGCCGGCGGA AGAAGGAAGG
1251 AGAATACAAC GTCCAGCAAC AGTGCCCAGG CTACTACCAG TCACACCTAG
1301 ACCTGGAGGA TCTGCAATGA CTGGAATTG CCGGTGCCTG GGGTGCCTTT
1351 CCCCAGCCA GGGTCCAAAG AAGCTTGGCT GGGGCAGAAA TAAACCATAT
1401 TGGTCGGAAA AAAAAAAAAA AA

TABLE 18

Carboxy Terminal Amino Acid Sequence
(SEQ ID NO: 148)

1 AMGYHLKTLT LNFTISNLQY SPDMGKGSAT FNSTEGVLQH LLRPLFQKSS
51 MGPFYLGCQL ISLRPEKDGA ATGVDTTCTY HPDPVGPGLD IQQLYWELSQ
101 LTHGVTQLGF YVLRDLSLFI NGYAPQNLSI RGEYQINFHI VWNLSNPDP
*
151 TSSEYITLLR DIQDKVTTLY KGSQ LHD TFR FCLVTNLTMD SVLVTVKALF
201 SSNLDPSLVE QVFLDKTLNA SFHWLGSTYQ LVDIHVTEME SSVYQPTSSS
251 STQH FYLNFT ITNLPYSQDK AQP GTTNYQR NKR NIEDALN QLFRNSSIKS
301 YFSDCQVSTF RSVPNRHHTG VDSL CNFSPL ARRVD RVAIY EEFLRMTRNG
351 TQLQNFTLDR SSVLVDGYSP NRNEPLTGNS DLPF WAVILI GLAGLLGLIT
401 CLICGVLVTT RRRKKEGEYN VQQQCPGYQ SHLDLEDLQ

TABLE 19A

Serine/Threonine O-glycosylation Pattern Predicted for the
Amino Terminal End of the CA125 Molecule
(SEQ ID NO: 149)

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SEQ ID NO: 149 Length: 1799

10 RTDGIMEHITKIPNEAAHRTIRPVKGPQTSTSPASPKGLHTGGTKRMETTTTALKTTTALKTTSRATLTTSVYTPTLG 80
TLTPLNASRQMASTILTEMMITTPYVFPDVPETTSLSLATS LGAETSTALPRTTPSVLNRESETTASLVSRSGAERSPVIQ 160
TLDVSSSEPDTTASWVIHPAETIPTVSKTTPNFHSELDTVSSTATSHGADVSSAIPNTNISPSELDALTPLVTISGTDTS 240
TTFPTLTSPHETETRTTWLTHPAETSSITPTIPNFHSHESDATPSIATSPGAETSSAIPIMTVSPGAEDLVTSQVTSS 320
GTDNRMTIPTLTLSPEGPKTIASLVTHPEAQTSSAIPSTISPAVSRVLTSMVTS LAAKTSTTNRALTNSPGEPATTVSL 400
15 VTHPAQTSPTVPWTTISIFFHKSDDTTPSMTTSHGAESSAVPTPTVSTEVPGVVTPLVTSSRAVISTTIPILTSLPGEPE 480
TTPSMATSHGEEASSAIPPTVSPGVPGVVTSLVTSSRAVSTTIPILTSLGEPETTPSMATSHGTEAGSAVPTVLPEV 560
PGMVTSLVASSRAVSTTTLPTLTSLPGEPEPTTPSMATSHGAEEASSTVPTVSPGVPGVVTSLVTSSSGVNSTSIPTLILSP 640
GELETTSPMATSHGAEEASSAVPTPTVSPGVSGVVTPLVTSSRAVSTTIPILTSLSSSEPETTPSMATSHGVEASSAVLTV 720
SPEVPGMVTSLVTSSRAVSTTIPILTSLSSSEPETTPSMATSHGVEASSAVLTV 800
LTVASSQPETIDSWVAHPGTEASSVPTLTSTGEPEFTNISLVTHPAESSSTLPRTTSRFSHSELDTMPSTVTSPEAESS 880
20 SAISTTISP GIPGVLTSVLTSSGRDISATFPTVPESPHESEATASWVTHPAVTSTTVPRTPPNYSHSEPDTPPSIATSPG 960
AEATSDFPITITVSPDVPDMVTSQVTSSGTDTSITIPILTSLSSSEPETTPSFITYSETHTSSAIPTLVPSPGASKMLTSLV 1040
ISSGTDSTTTFTLTETPYEPETTAIQLIHPAETNTMVPRTTPKFHSHKSDDTLPVAITSPGPEASSAVSTTTISPDMSD 1120
25 LVTSVLPSSGTDSTTFTLTETPYEPETTAIQLIHPAETNTMVPRTTPKFHSHKSDDTLPVAITSPGPEASSAVSTTTISPDMSD 1200
PSIPGVVTSQVTSSATDTSTAIPTLTSPGEPETTASSATHPGTGTGTVPIRTVPSSEPDTMASWVTHPPQTSTPVSRT 1280
TSSFSHSSPDATPVMATSPRTEASSAVLTTISPGAPEMVTSQITSSGAATSTTVPTLTHSPGMPETTALLSTHPRTETSK 1360
TFPASTVFPQVSETTASLTIRPGAETSTALPTQTTSLSLFTLLVGTSTSRVDLSPTASPGVSAKTAPLSTHPGTETSTMIPT 1440
STLSLGLLETTGLLATSSAETSTSTLTLSVPAVSGLSASITTDKPKQTVTWNTESTSPSVTSVGPPESRTVTGTMT 1520
LIPSEMPPTPKTSHGEGVSPPTILRTMVEATNLATTGSSPTVAKTTTFTNTLAGSLFTPLTTPGMSTLASESVTSRTSY 1600
30 NHRSWISTTSSYNRRYWT PATSTPVTSTFSPGISTSSIPSSAATVPFMPVFTLNFTITNLQYEEDMRHPGSRKFNATER 1680
ELQGLLKPLFRNSSLEYLYSGCRLASLRPEKDSSAMAVDAICTHRPDPEDLGLDRERLYWELSNLTNGIQELGPYTLDRN 1760
SLYVNGFTHRSMPTTSTPGTSTVDVGTSGTPSSSPST

TABLE 19B

.....T.....TSTS.....TTT.....TTTT.....TT.....TT...T.... 80
.....ST...TT..... 160
.....S.....T.....T.S.....T.....S.....S.T..S 240
T...T.T.....TSS...T.....S.T.S.TS.....S.....T.....T..TS. 320
.....T.S.....T.S.....TSS...TST.....T.....STT...T.S....TT.S. 400
.....T.S.....T.S.....TSS...TST.....T.....T.....T.S.... 480
.....T.S.....T.S.....TSS...TST.....T.....T.....T.S.... 560
.....T.S.....T.S.....TSS...TST.....T.....T.....T.S.... 640
.....T.S.....T.S.....TSS...TST.....T.....T.....T.S.... 720
.....T.S.....T.S.....TSS...TST.....T.....T.....T.S.... 800
.....T.S.....T.S.....TSS...TST.....T.....T.....T.S.... 880
45 S.....S.....STT..T.T.SS...TT.....S.....S.....ST.T.....S 960
.....S.....SS...T.....T.....S.....T.....TSTT...TT...S.S...T.S.TS.. 1040
S...TT.S.....S.....T.....S.T...T...TSTT...TT...S.S...T.S.TS.. 1120
.....TS.....T.....T...TS.....T...TT.....S.....S.....SS...TT..... 1200
.....S.T.STTT..T.T.T.....T...TT.....S.....S.....TS.....S...TT.. 1280
50S.T..STT..T.S.T.....TT...T.....ST.....T.SS...T.S...TST..S.T 1360
.....S.....T...TS...T.TST...T.T.S.....TT.SS.T.....T.SS...T.S...TST..S.T 1440
TSS.S.SS...T...TS...T.SS...T.S.....T...TS...TSTT...T.S.....ST...T.S. 1520
.....ST.....S.TT...T.....ST...T.TT.S.....T.S.....S.....ST...T.S.T 1600
ST.....T.S...TSTS...T.....S.S.S.T...T.TS...T.S.S.TS.....S.....T 1680

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TABLE 19B-continued

5	Serine/Threonine O-glycosylation Pattern Predicted for the Amino Terminal End of the CA125 Molecule	
10	<div> <div> <div>...</div> <div>S...</div> <div>T...</div> <div>S...</div> <div>T...</div> <div>TT</div> <div>SS</div> <div>T</div> <div>T...ST..S</div> </div> <div> <div>.....</div> <div>TST..TST.S...</div> <div>STSS..SST</div> <div>.....</div> <div>.....</div> <div>.....</div> <div>TTST...ST....TS.T.SSS.S.T</div> </div> </div>	<div>1600</div> <div>1680</div> <div>1760</div>

00065733 000704

TABLE 20

Nucleotide and Amino Acid Sequences of Recombinant CA125 Repeat Showing Peptides
(Underlined 1-4) which are Antigenically Matched for Immune Stimulation of
Patients with the HLA-2 Histocompatibility Subtype

CA 125 Recombinant Nucleotide and Amino Acid Sequences
(SEQ ID NO: 151 and SEQ ID NO: 152, respectively)

CA 125 Recombinant Nucleotide (Anti-Sense Strand) Sequence (SEQ ID NO: 153)
Peptide 1 (SEQ ID NO: 154); Peptide 2 (SEQ ID NO: 155);
Peptide 3 (SEQ ID NO: 156) and Peptide 4 (SEQ ID NO: 157)

ATGAGAGGATCGCATCACCATCACCATCACGGATCCATGGGCCACACAGAGCCTGGCCCT
1 -----+-----+-----+-----+-----+ 60
TACTCTCCTAGCGTAGTGGTAGTGGTAGTGCCTAGGTACCCGGTGTGTCTCGGACCGGGA
M R G S H H H H H G S M G H T E P G P -
CTCCTGATACCATTCACTTTCAACTTTACCATCACCAACCTGCATTATGAGGAAAACATG
61 -----+-----+-----+-----+-----+ 120
GAGGACTATGGTAAGTGAAAGTTGAAATGGTAGTGGTTGGACGTAATACTCCTTTGTAC
L L I P F T F N F T I T N L H Y E E N M -
CAACACCCTGGTTCCAGGAAGTTCAACACCACGGAGAGGGTTCTGCAGGGTCTGCTCAAG
121 -----+-----+-----+-----+-----+ 180
GTTGTGGGACCAAGGTCCTTCAAGTTGTGGTGCCTCTCCCAAGACGTCCCAGACGAGTTC
Q H P G S R K F N T T E R V L Q G L L K -
CCCTTGTTCAGAACACCAGTGTGGCCCTCTGTACTCTGGCTGCAGACTGACCTTGCTC
181 -----+-----+-----+-----+-----+ 240
GGGAACAAGTTCTTGTGGTCACAACCGGGAGACATGAGACCGACGTCTGACTGGAACGAG
P L F K N T S V G P L Y S G C R L T L L -
AGACCTGAGAAGCATGAGGCAGCCACTGGAGTGGACACCATCTGTACCCACCGGTTGAT
241 -----+-----+-----+-----+-----+ 300
TCTGGACTCTTCGTACTCCGTCCGTGACCTCACCTGTGGTAGACATGGGTGGCGCAACTA
R P E K H E A A T G V D T I C T H R V D -
CCCATCGGACCTGGACTGGACAGAGCGGCTATACTGGGAGCTGAGCCAGCTGACCAAC
301 -----+-----+-----+-----+-----+ 360
GGGTAGCCTGGACCTGACCTGTCTCTCGCCGATATGACCCTCGACTCGGTGCGACTGGTTG
P I G P G L D R E R L Y W E L S Q L T N -
AGCATCACAGAGCTGGGACCCTACACCCTGGACAGGGACAGTCTCTATGTCAATGGCTTC
361 -----+-----+-----+-----+-----+ 420
TCGTAGTGTCTCGACCCTGGGATGTGGGACCTGTCCCTGTCAGAGATACAGTTACCGAAG

TABLE 20 (continued)

5 Nucleotide and Amino Acid Sequences of Recombinant CA125 Repeat Showing Peptides
(Underlined 1-4) which are Antigenically Matched for Immune Stimulation of
Patients with the HLA-2 Histocompatibility Subtype

10 CA 125 Recombinant Nucleotide and Amino Acid Sequences
(SEQ ID NO: 151 and SEQ ID NO: 152, respectively)
CA 125 Recombinant Nucleotide (Anti-Sense Strand) Sequence (SEQ ID NO: 153)
Peptide 1 (SEQ ID NO: 154); Peptide 2 (SEQ ID NO: 155);
Peptide 3 (SEQ ID NO: 156) and Peptide 4 (SEQ ID NO: 157)

15 S I T E L G P Y ² T L D R D S L Y V N G F -
AACCTCTGGAGCTCTGTGCCAACACCAGCACTCCTGGGACCTCCACAGTGCACCTGGCA
421 -----+-----+-----+-----+-----+ 480
TTGGGAGCCTCGAGACACGGTTGGTGGTCGTGAGGACCCTGGAGGTGTCACGTGGACCGT
20 N P R S S V P T T S T P G T S T V H L A -
ACCTCTGGGACTCCATCCTCCCTGCCT
25 481 -----+-----+----- 507
TGGAGACCCTGAGGTAGGAGGGACGGA
T S G T P S S L P -

30 (SEQ ID NO: 154)
Peptide 1 R L Y W E L S Q L

35 (SEQ ID NO: 155)
Peptide 2 T L D R D S L Y V

40 (SEQ ID NO: 156)
Peptide 3 V L Q G L L K P L

45 (SEQ ID NO: 157)
Peptide 4 Q L T N S I T E L

TABLE 21

CA125 Protein Sequence
(SEQ ID NO: 162)

5	1	MEHITKIPNE	AAHRGTIRPV	KGPQTSTSPA	SPKGLHTGGT	KRMETTTTAL	A
	51	KTTTTALKTT	SRATLTTSVY	TPTLGLTLPL	NASRQMASTI	LTEMMITTPY	m
	101	VFPDVPETTS	SLATSLGAET	STALPRTTPS	VLNRESETTA	SLVSRSGAER	i
10	151	SPVIQTLDVD	SSEPDTTASW	VIHPAETIPT	VSKTTPNFFH	SELDTVSSTA	n
	201	TSHGADVSSA	IPTNISPSEL	DALTPLVTIS	GTDSTTFPPT	LTKSPHETET	o
	251	RTTWLTHPAE	TSSTIPRTIP	NFSHHESDAT	PSIATSPGAE	TSSAIPIMTV	
	301	SPGAEDLVTS	QVTSSGTDNR	MTIPTLTLS	GEPKTIASLV	THPEAQTSSA	
	351	IPSTTISPAV	SRLVTSMTVS	LAAKTSTTNR	ALTNSPGEP	TTVSLVTHPA	
15	401	QTSPTVPWTT	SIFFHSKSDT	TPSMTTSHGA	ESSSAVPTPT	VSTEVPGVVT	T
	451	PLVTSSRAVI	STTIPILTLS	PGEPTTPSM	ATSHGEEASS	AIPTPTVSPG	e
	501	VPGVVTSLVT	SSRAVTSTTI	PILTFSLGEP	ETTPSMATSH	GTEAGSAVPT	r
	551	VLPEVPGMVT	SLVASSRAVT	STTLPTLTLS	PGEPTTPSM	ATSHGAEASS	m
	601	TVPTVSPPEV	GVVTSVLTSS	SGVNSTSIPT	LILSPGELET	TPSMATSHGA	i
20	651	EASSAVPTPT	VSPGVSGVVT	PLVTSSRAVT	STTIPILTLS	SSEPPTTPSM	n
25	701	ATSHGVEASS	AVLTVSPEVP	GMVTSVLTSS	RAVTSTTIPT	LTSSDEPET	a
	751	TTSLVTHSEA	KMISAIPTLA	VSPTVQGLVT	SLVTSSGSET	SAFSNLTVAS	l
	801	SQPETIDSWV	AHPGTEASSV	VPTLTVSTGE	PFTNISLVTH	PAESSSTLPR	
	851	TTSRFSHSEL	DTMPSTVTSP	EAESSAIST	TISPGIPGVL	TSLVTSSGRD	
	901	ISATFPTVPE	SPHESEATAS	WVTHPAVTST	TVPRTPNYS	HSEPDTTPSI	
	951	ATSPGAEATS	DFPTITVSPD	VPDMVTSQVT	SSGTDTSITI	PTLTLSSGEP	
	1001	ETTTSFITYS	ETHTSSAIPT	LPVSPGASKM	LTSLVISSGT	DSTTFPTLT	
	1051	ETPYEPETTA	IQLIHPAETN	TMVPRTPPKF	SHSKSDTTL	VAITSPGPEA	D
	1101	SSAVSTTTIS	PDMSDLVTSL	VPSSGTDIST	TFPTLSETPY	EPETTATWLT	o
30	1151	HPAETSTTVS	GTIPNFSHRG	SDTAPSMVTS	PGVDTRSGVP	TTTIPPSIPG	m
	1201	VVTSQVTSSA	TDSTAIPTL	TPSPGEPETT	ASSATHPGTQ	TGFTVPIRTV	a
	1251	PSSEPDTMAS	WVTHPPQTST	PVSRTTSSFS	HSSPDATPVM	ATSPRTEASS	i
	1301	AVLTITISPGA	PEMVTSQLTS	SGAATSTTV	TLTHSPGMPE	TTALLSTHPR	n
	1351	TETSKTFPAS	TVFPQVSETT	ASLTIRPGAE	TSTALPTQTT	SSLFTLLVTG	
35	1401	TSRVLSPTA	SPGVSAKTAP	LSTHPGTETS	TMIPSTLSL	GLLETTGLLA	
	1451	TSSSAETSTS	TLTLTVSPAV	SGLSSASITT	DKPQTVTSWN	TETSPSVTSV	
	1501	GPPEFSRTVT	GTTMTLIPSE	MPTPPKTSHG	EGVSPPTILR	TTMVEATNLA	
	1551	TTGSSPTVAK	TTTTFNTLAG	SLFTPLTPG	MSTLASESVT	SRTSYNHRWS	
40	1601	ISTTSSYNRR	YWTPATSTPV	TSTFSPGIST	SSIPSSSTA		

TABLE 21 - continued

CA125 Protein Sequence
(SEQ ID NO: 162)

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AT VPFMVPTLN

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1651 FTITNLQYEE DMRHGPSRKFNATERELQGL LKPLFRNSSL EYLYSGCRLA
 1701 SLRPEKDSSA MAVDAICTHR PDPEDLGLDR ERLYWELSNL TNGIQELGPY
 1751 TLDNRSLYVN GFTHRSSMPT TSTPGTSTVD VGTSGTPSSS PSPTAAGPLL
 1801 MPFTLNFTIT NLQYEE DMRR TGSRKFNTE SVLQGLLKPL FKNTSVGPLY
 1851 SGCRLTLRPE EKDGAATGVD AICTHRLDPK SPGLNREQLY WELSKLTNDI
 1901 EELGPYTLDR NSLYVNGFTH QSSVSTSTP GTSTVDLRTS GTPSSLSSPT
 1951 IMAAGPLLVP FTNLFTITNL QYGEDMGHPG SRKFNTTERV LQGLLGPIFK
 2001 NTSVGPLYSG CRLTSLRSEK DGAATGVDAI CIHHLDPKSP GLNRERLYWE
 2051 LSQLTNGIKE LGPYTLDRNS LYVNGFTHRT SVPTSSTPGT STVDLGTSGT
 2101 PPSLPSPATA GPLLVLFITL FTITNLKYEE DMHRPGSRKF NTERVLQTL
 2151 LGPMFKNTSV GLLYSGCRLT LLRSEKDGA TGVDAICTHR LDPKSPGLDR
 2201 EQLYWELSQL TNGIKELGPY TLDNRSLYVN GFTHWIPVPT SSTPGTSTVD
 2251 LSGTTPSSLP SPTAAGPLLVP PFTLNFTITN LQYEE DMHHP GSRKFNTTER
 2301 VLQGLLGPMF KNTSVGLLYS GCRLTLRSE KDGAATGVDA ICTHRLDPKS
 2351 PGVDREQLYW ELSQLTNGIK ELGPYTLDRN SLYVNGFTHQ TSAPNTSTPG
 2401 TSTVDLGTSG TPSSLPSPS AGPLLVPTL NFTITNLQYE EDMRHPGSRK
 2451 FNTTERVLQG LLKPLFKSTS VGPLYSGCRL TLLRSEKDGA ATGVDAICTH
 2501 RLDPKSPGVD REQLYWELSQ LTNGIKELGP YTLDRNSLYV NGFTHQTSAP
 2551 NTSTPGTSTV DLGTSGTPSS LPSPTSAGPL LVPFTLNFTI TNLQYEE DMH
 2601 HPGSRKFNTT ERVLQGLLGP MFKNTSVGLL YSGCRLTLR PEKNGAATGM
 2651 DAICSHRLDP KSPGLNREQL YWELSQLTHG IKELGPYTLD RNSLYVNGFT
 2701 HRSSVAPTST PGTSTVDLGT SGTPSSLPSP TAVPLLVPF TLNFTITNLQ
 2751 YGEDMRHGPS RKFNTERVL QGLLGPLFKN SSVGPLYSGC RLISLRSEKD
 2801 GAATGVDAIC THHLNPQSPG LDREQLYWQL SQMTNGIKEL GPYTLDRNSL
 2851 YVNGFTHRSS GLTSTPWTS TVDLGTSGTP SPVPSPTTAG PLLVPFTLNF
 2901 TITNLQYEE DMHRPGSRKF ATERVLQGLL SPIFKNSSVG PLYSGCRLTS
 2951 LRPEKDGAAT GMDAVCLYHP NPKRPGLDRE QLYWELSQL HNITELGPYS
 3001 LDRDSLYVNG FTHQNSVPTT STPGTSTVYW ATTGTPSSFP GHTEPGPLLI
 3051 PFTFNFTITN LHYEENMQHP GSRKFNTTER VLQGLLKPLF KNTSVGPLYS
 3101 GCRLTSLRPE KDGAATGMDA VCLYHPNPKR PGLDREQLYC ELSQLTHNIT
 3151 ELGPYSLDRD SLYVNGFTHQ NSVPTTSTPG TSTVYWATTG TPSSFPGHTE
 3201 PGPLLIPTFT NFTITNLHYE ENMQHPGSRK FNTTERVLQG LLKPLFKNTS
 3251 VGPLYSGCRL TLLRPEKHEA ATGVDTICTH RVDPIGPGLD RERLYWELSQ
 3301 LTNSITELGP YTLDRDSLYV NGFNPRSSVP TTSTPGTSTV HLATSGTPSS
 3351 LPGHTAPVPL LIPFTLNFTI TNLHYEENMQ HPGSRKFNTT ERVLQGLLKP
 3401 LFKNTSVGPLY YSGCRLTLR PEKHEAATGV DTICTHRVDP IGPGLDREXL
 3451 YWELSLTXIX ELGPYXLD RXSLYVNGFX XXXXXXSTST PGTSXVXLXT
 3501 SGTPXXXPPX TSAGPLLVPF TLNFTITNLQ YEEDMHHPGS RKFNTERVL
 3551 QGLLGPMFKN TSVGLLYSGC RLTLRPEKN GAATGMDAIC SHRLDPKSPG
 3601 LDREQLYWEL SQLTHGIKEL GPYTLDRNSL YVNGFTHRSS VAPTSTPGTS
 3651 TVDLGTSGTP SSLPSPTTAV PLLVPFTLNF TITNLQYGED MRHPGSRKFN
 3701 TTERVLQGLL GPLFKNSSVG PLYSGCRLIS LRSEKDGAAT GVDAICTHHL
 3751 NPQSPGLDRE QLYWQLSQMT NGIKELGPYT LDRNSLYVNG FTHRSSGLTT
 3801 STPWTSTVDL GTSGTPSPVP SPTTAGPLLVP PFTLNFTITN LQYEE DMHRP
 3851 GSRKFNATER VLQGLLSPIF KNSSVGPLYG GCRLTSLRPE KDGAATGMDA
 3901 VCLYHPNPKR PGLDREQLYW ELSQLTHNIT ELGPYSLDRD SLYVNGFTHQ
 3951 SSMTTTRTPD TSTMHLATSR TPASLSGPTT ASPLLVLFTI NCTITNLQYE

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TABLE 21 - continued

CA125 Protein Sequence
(SEQ ID NO: 162)

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4001 EDMRRTGSRK FNTMESVLQG LLKPLFKNTS VGPLYSGCRL TLLRPKKDGA
4051 ATGVDAICTH RLDPKSPGLN REQLYWELSK LTNDIEELGP YTLDRNSLYV
4101 NGFTHQSSVS TTSTPGTSTV DLRTSGTPSS LSSPTIMXXX PLLXPFTLNF
4151 TITNLXYEEX MXXPGSRKFN TTERVLQGLL RPLFKNTSVS SLYSGCRLTL
4201 LRPEKDGAAT RVDAACTYRP DPKSPGLDRE QLYWELSQT HSITELGPYT
4251 LDRVSLYVNG FNPRSSVPTT STPGTSTVHL ATSGTPSSLP GHTXX XPLL
4301 XPFTLNFTIT NLXYEEXMXX PGSRKFNTTE RVLQGLLKPL FRNSSLEYLY
4351 SGCRLASLRP EKDSSAMAVD AICTHRPDPE DLGLDRERLY WELSNLTNGI
4401 QELGPYTLDL NSLYVNGFTH RSSFLTSTP WTSTVDLGS GTPSPVPSPT
4451 TAGPLLVPT LNFITITNLQ EEDMHRPGSR RFNTTERVLQ GLTTPLFKNT
4501 SVGPLYSGCR LTLRPEKQE AATGVDICT HRVDPIGPGL DRERLYWELS
4551 QLTNSITELG PYTLDRDSL YVNGFNPWSSV PTTSTPGTST VHLATSGTPS
4601 SLPGHTAPVP LLIPFTLNFT ITDLHYEENM QHPGSRKFNT TERVLQGLLK
4651 PLFKSTSVGP LYSGCRLTLL RPEKHGAATG VDAICTLRD PTGPGLDRER
4701 LYWELSQTIN SVTELGPYTL DRDSL YVNGF THRSSVPTTS IPGTSAVHLE
4751 TSGTPASLPG HTAPGPLLV FTLNFTITNL QYEEDMRHPG SRKFSTTERV
4801 LQGLLKPLFK NTSVSSLYSG CRLTLRPEK DGAATRVDAV CTHRPDPKSP
4851 GLDRERLYWK LSQTHGITE LGPYTLDRHS LYVNGFTHQS SMTTTRTPDT
4901 STMHLATSRT PASLSGPTTA SPLVLFTIN FTITNQRYEE NMHPGSRKF
4951 NTERVLQGL LRPVFKNTSV GPLYSGCRLT LLRPKKDGAA TKVDAICTYR
5001 PDPKSPGLDR EQLYWELSQT HSITELGPY TQDRDSL YVN GFTHRSSVPT
5051 TSIPGTSAVH LETSGTPASL PGHTAPGPLL VPFTLNFTIT NLQYEEDMRH
5101 PGSRKFNTTE RVLQGLLKPL FKSTSVGPLY SGCRLTLR EKRGAATGVD
5151 TICTHRLDPL NPGLDREQLY WELSKLTRGI IELGPYLLDR GSLYVNGFTH
5201 RTSVPTTSTP GTSTVDLGS GTPFSLPSA XXXPLLXPFT LNFITITNLXY
5201 EEXMXXPGSR KENTTERVLQ TLLGPMFKNT SVGLLYSGCR LTLRSEKDG
5251 AATGVDAICT HRLDPKSPGV DREQLYWELS QLTNGIKELG PYTLDRNSLY
5301 VNGFTHWIPV PTSSTPGTST VDLGSGTPSL PSSPTTAGPL LVPFTLNFTI
5351 TNLKYEEDMH CPGSRKFNTT ERLQSLGMP MFKNSTSVGPL YSGCRLTLR
5401 SEKDGAATGV DAICTHRLDP KSPGV DREQL YWELSQTNG IKELGPYTL
5451 RNSLYVNGFT HQTSAPNTST PGTSTVDLGT SGTPSSLPSP TXXXPLLXPF
5501 TLNFTITNLX YEEXMXXPGS RKFNTTERVL QGLLXPFXKX TSVGXLYSGC
5551 RLTLRKEKX KAATXVDXXC XXXXDPXXPG LDREXLYWEL SXLTXXIXEL
5601 GPYXLDRXSL YVNGFTHWIP VPTSSTPGTS TVDLGSGTPS SLPSPTTAGP
5651 LLVPFTLNFT ITNLKYEEDM HCPGSRKFNT TERVLQSLG PMFKNTSVGP
5701 LYSGCRLTSL RSEKDGAATG VDAICTHRVD PKSPGV DREQ LYWELSQTIN
5751 GIKELGPYTL DRNSLYVNGF THQTSAPNTS TPGTSTVDLG TSGTPSSLP

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TABLE 21 - continued

CA125 Protein Sequence
(SEQ ID NO: 162)

5801 PTSAGPLLVP FTLNFTITNL QYEEDMHHPG SRKFNTTTERV LQGLLGPMPFK
 5851 NTSVGLLYSG CRLTLLRPEK NGAATGMDAI CTHRLDPKSP GLDREXLYWE
 5901 LSXLTXIXE LGPYXLDXRS LYVNGFXXXX XXXXTSTPGT SXVXLXTSGT
 5951 PXXXXPXTXX XPLLXPFTLN FTITNLXYEE MXXPGRKRF NTERVLQGL
 6001 LKPLFRNSSL EYLYSGCRLA SLRPEKDSSA MAVDAICTHR PDPEDLGLDR
 6051 ERLYWELSNL TNGIQELGPY TLDRLSLYVN GFTHRSSMPT TSTPGTSTVD
 6101 VGTSGTPSSS PSPTTAGPLL IPFTLNFTIT NLQYGEDMGH PGSRKFNTTE
 6151 RVLQGLLGPY FKNTSVGPLY SGCRLTSLRS EKDGAATGVD AICIHHLDPK
 6201 SPGLNRERLY WELSQLTNGI KELGPYTLDR NSLYVNGFTH RTSVPTTSTP
 6251 GTSTVDLGTG GTPFSLPSPA TAGPLLVLF LFTITNLKY EEDMHRPGSR
 6301 KFNTTTERVLQ TLLGPMFKNT SVGLLYSGCR LTLRSEKDG AATGVDICT
 6351 HRLDPKSPGL DREXLYWELS XLTXIXELG PYXLDXSLY VNGFXXXXXX
 6401 XXTSTPGTSX VXLXTSGTPX XXPXTXXXP LLXPFTLNFT ITNLXYEEXM
 6451 XXPGSRKFNT TERVLQGLR PVFKNTSVGP LYSGCRLTLL RPKKDGAATK
 6501 VDAICTYRPD PKSPGLDREQ LYWELSQLTH SITELGPTYQ DRDSLTVNGF
 6551 THRSSVPTTS IPGTSVHLE TTGTPSSFPG HTEPGPLLIP FTFNFTITNL
 6601 RYEENMQHPG SRKFNTTTERV LQGLLTPLFK NTSVGPLYSG CRLTLLRPEK
 6651 QEAATGVDTI CTHRVDPGIP GLDRERLYWE LSQLTNSITE LGPYTLDRDS
 6701 LYVDGFNPWS SVPTTSTPGT STVHLATSGT PSPLPGHTAP VPLLIPFTLN
 6751 FTITDLHYEE NMQHPGSRKF NTERVLQGL LKPLFKSTSV GPLYSGCRLT
 6801 LLRPEKHGAA TGVDICTLR LDPTGPGGLDR ERLYWELSQL TNSITELGPY
 6851 TLDRLSLYVN GFNPWSSVPT TSTPGTSTVH LATSGTPSSL PGHTAGPLL
 6901 VPFTLNFTIT NLKYEEDMHC PGSRKFNTTE RVLQSLHGM FKNTSVGPLY
 6951 SGCRLTLLRS EKDGAATGVD AICTHRLDPK GTSXVXLXTS GTPXXXPXT
 7001 XELGPYXLDX XSLYVNGFXX XXXXXXTSTP KFNTERVLQ GLLXPXFKXT
 7051 XXXPLLXPFT LNFTITNLXY EEXMXXPGSR KFNTERVLQ GLLXPXFKXT
 7101 SVGLYSGCR LTLRKEKXX AATXVDXXCX XXXDPXPG L DREXLYWELS
 7151 XLTNSITELG PYTLDRDSLY VNGFTHRSSM PTTIPGTSV VHLETSGTPA
 7201 SLPGHTAPGP LLVPFTLNFT ITNLQYEEDM RHPGSRKFNT TERVLQGLL
 7251 PLFKSTSVGP LYSGCRLTLL RPEKGAATG VDTICTHRLD PLNPGLDREX
 7301 LYWELSLTX XIXELGPYXL DRXSLYVNGF XXXXXXXXTS TPGTSXVXLX
 7351 TSGTPXXXPX XTXXXPLLXP FTLNFTITNL XYEEXMXXPG SRKFNTTTERV
 7401 LQGLLXPXFK XTSVGLYSG CRLTLLRKEK XXAATXVDXX CXXXDPXXP
 7451 GLDREXLYWE LSXLTXIXE LGPYXLDXRS LYVNGFHPRS SVPTTSTPGT
 7501 STVHLATSGT PSSLPHTAP VPLLIPFTLN FTITNLHYEE NMQHPGSRKF
 7551 NTERVLQGL LGPMFKNTSV GLLYSGCRLT LLRPEKNGAA TMDAICSHR
 7601 LDPKSPGLDR EXLYWELSLX TXXIXELGPY XLDRLSLYVN GFXXXXXXX
 7651 TSTPGTSXVX LXTSGTPXXX PXXTXXXPLL XPFTLNFTIT NLXYEEXMXX
 7701 PGSRKFNTTE RVLQGLLXP FKXTSVGLY SGCRLTLLRX EKXXAATXVD
 7751 XXCXXXXDPX XPGLDREXLY WELSLTXIXE XELGPYXLDX XSLYVNGFTH
 7801 QNSVPTTSTP GTSTVYWATT GTPSSFPGHT EPGPLLIPFT FNFTITNLHY
 7851 EENMQHPGSR KFNTERVLQ GLLTLPFKNT SVGPLYSGCR LTLRPEKQE
 7901 AATGVDTICT HRVDPIGPGL DREXLYWELS XLTXIXELG PYXLDXSLY
 7951 VNGFXXXXXX XXTSTPGTSX VXLXTSGTPX XXPXTXXXP LLXPFTLNFT
 8001 ITNLXYEEXM XXPGSRKFNT TERVLQGLLX PXFKXTSVGX LYSGCRLTLL
 8051 RXEKXXAATX VDXCXXXXD PXXPGLDREX LYWELSLTX XIXELGPYXL
 8101 DRXSLYVNGF THRSSVPTTS SPGTSTVHLA TSGTPSSLPG HTAPVPLLIP
 8151 FTLNFTITNL HYEENMQHPG SRKFNTTTERV LQGLLKPFLK STSVGPLYSG
 8201 CRLTLLRPEK HGAATGVDAI CTLRLDPTGP GLDREXLYWE LSXLTXIXE
 8251 LGPYXLDXRS LYVNGFXXXX XXXXTSTPGT SXVXLXTSGT PXXXXPXTXX
 8301 XPLLXPFTLN FTITNLXYEE MXXPGRKRF NTERVLQGL LXPXFKXTSV

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TABLE 21 - continued

CA125 Protein Sequence
(SEQ ID NO: 162)

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8351	GXLYSGCRLT	LLRXEKXAA	TXVDXXCXX	XDPXXPGLDR	EXLYWELSXL	
8401	TXXIXELGPY	XLDXSLYVN	GFTHRTSVPT	TSTPGTSTVH	LATSGTPSSL	
8451	PGHTAPVPLL	IPFTLNFTIT	NLQYEEDMHR	PGSRKFNTTE	RVLQGLLSPI	
8501	FKNSSVGPLY	SGCRLTSLRP	EKDGAATGMD	AVCLYHPNPK	RPGLDREQLY	
8551	CELSQLTHNI	TELGPSYSLDR	DSLYVNGFTH	QNSVPTTSTP	GTSTVYWATT	
8601	GTPSSFPGHT	XXXPLLXPFT	LNFTITNLXY	EEXMXXPGSR	KFNTTERVLQ	
8651	GLLXPXFKXT	SVGXLYSGCR	LTLRLXKXX	AATXVDXXCX	XXXDPXXPGL	
8701	DREXLYWELS	XLTXIXELG	PYXLDXSLY	VNGFTHWSSG	LTTSTPWTST	
8751	VDLGTSGTPS	PVPSPTTAGP	LLVPFTLNFT	ITNLQYEEDM	HRPGSRKFNA	
8801	TERVLQGLLS	PIFKNTSVGP	LYSGCRLTLL	RPEKQEAATG	VDTICTHRVD	
8851	PIGPGLDREX	LYWELSXLTX	XIXELGPYXL	DRXSLYVNGF	XXXXXXXXTS	
8901	TPGTSXVXLX	TSGTPXXXPX	XTXXXPLLXP	FTLNFTITNL	XYEEXMXXPG	
8951	SRKFNTTERV	LQGLLXPXFK	XTSVGXLYSG	CRLTLRLXKX	XXAATXVDXX	
9001	CXXXXDPXXP	GLDREXLYWE	LSXLTXIXE	LGPYXLDXRS	LYVNGFTHRS	
9051	FGLTTSTPWT	STVDLGTSGT	PSPVPSPTTA	GPLLVPFTLN	FTITNLQYEE	
9101	DMHRPGSRKF	NTTERVLQGL	LTPLFRNTSV	SSLYSGCRLT	LLRPEKDGAA	
9151	TRVDAVCTHR	PDPKSPGLDR	EXLYWELSXL	TXXIXELGPY	XLDXSLYVN	
9201	GFXXXXXXXX	TSTPGTSXVX	LXTSGTPXXX	PXXTXXXPLL	XPFTLNFTIT	
9251	NLYEEXMXX	PGSRKFNTTE	RVLQGLLXPX	FKXTSVGXLY	SGCRLTLRLX	
9301	EKXXAATXVD	XXCXXXXDPX	XPGLDREXLY	WELSXLTXXI	XELGPYXLDL	
9351	XSLYVNGFTH	WIPVPTSSTP	GTSTVDLGS	TPSSLPSPTT	AGPLLVPFTL	
9401	NFTITNLQYG	EDMGHPGSRK	FNTTERVLQG	LLGPIFKNTS	VGPLYSGCRL	
9451	TSLRSEKDGA	ATGVDAICIH	HLDPKSPGLD	REXLYWELS	LTXXIXELGP	
9501	YXLDXSLYV	NGFXXXXXXX	XTSTPGTSXV	XLXTSGTPXX	XPXTXXXPL	
9551	LXPFTLNFTI	TNLXYEEXMX	XPGRKFNTT	ERVLOGLLXP	XFXTSVGX	
9601	YSGCRLTLRL	XKXXAATXV	DXCXXXXDP	XXPGLDREXL	YWELSXLTX	
9651	IXELGPYXLD	RXSLYVNGFT	HQTFAPNTST	PGTSTVDLGT	SGTPSSLPS	
9701	TSAGPLLVPF	TLNFTITNLQ	YEEDMHHPGS	RKFNTTERVL	QGLLGPMPFK	
9751	TSVGLLYSGC	RLTLRLPEKN	GAATRVDAVC	THRPDPKSPG	LDREXLYWEL	
9801	SXLTXIXEL	GPYXLDXSL	YVNGFXXXXX	XXXTSTPGTS	XVXLXTSGTP	
9851	XXXPXXTAPV	PLLIPFTLNF	TITNLHYEEN	MQHPGSRKFN	TTERVLQGLL	
9901	RPLFKSTSVG	PLYSGCRLTL	LRPEKHGAAT	GVDAICTLRL	DPTGPGLDRE	
9951	RLYWELSQLT	NSVTELGPYT	LDRDSLTVNG	FTQRSSVPTT	SIPGTSAVHL	
10001	ETSGTPASLP	GHTAPGPLLV	PFTLNFTITN	LQYEVDMRHP	GSRKFNTTER	
10051	VLQGLLKPLF	KSTSVGPLY	GCRLTLRLPE	KRGAATGVD	ICTHRLDPLN	
10101	PGLDREQLYW	ELSKLTRGII	ELGPYLLDRG	SLYVNGFTHR	NFVPITSTPG	
10151	TSTVHLGTSE	TPSSLPRPIV	PGPLLVPFTL	NFTITNLQYE	EAMRHPGSRK	
10201	FNTTERVLQ	LLRPLFKNTS	IGPLYSSCRL	TLLRPEKDKA	ATRVDAICTH	
10251	HPDPQSPGLN	REQLYWELS	Q	LTHGITEG	YTLDRDSLTV	DGFTHWSPIP
10301	TTSTPGTSIV	NLGTSGIPPS	LPETXXXPL	LXPFTLNFTI	TNLXYEEXMX	
10351	XPGSRKFNTT	ERVLOGLLKP	LFKSTSVGPL	YSGCRLTLRL	PEKDGVA	TRV
10451	DAICTHRPDP	KIPGLDRQQL	YWELSQTLS	ITELGPYTL	RDSLTVNGFT	
10501	QRSSVPTTST	PGTFTVQPET	SETPSSLPGP	TATGPVLLPF	TLNFTITNLQ	
10551	YEEDMHRPGS	RKFNTTERVL	QGLLMPLFKN	TSVSSLYSGC	RLTLRLPEKD	
10601	GAATRVDAVC	THRPDPKSPG	LDRERLYWKL	SQLTHGITE	GPYTLDRHSL	
10651	YVNGFTHQSS	MTTTRTPDTS	TMHLATSRTP	ASLSGPTTAS	PLLVLFTINF	
10701	TITNLRYEEN	MHHPGSRKFN	TTERVLQGLL	RPVFKNTSVG	PLYSGCRLTL	
10751	LRPKKDGAAT	KVDAICTYRP	DPKSPGLDRE	QLYWELSQLT	HSITELGPYT	
10801	QDRDSLTVNG	FTQRSSVPTT	SVPGTPTVDL	GTSGTPVSKP	GPSAASPLL	
10851	LFTLNGTITN	LRYEENMQHP	GSRKFNTTER	VLQGLLRS	LKSTSVGPLY	
10901	GCRLTLRLPE	KDGTATGVDA	ICTHHPDPKS	PRLDREQLYW	ELSQLTHNIT	

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TABLE 21 - continued

CA125 Protein Sequence
(SEQ ID NO: 162)

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10951 ELGHYALDND SLFVNGFTHR SSVSTSTSPG TPTVYLGASK TPASIFGPSA
11001 ASHLLILFTL NFTITNLRYE ENMWPGSRKF NTTERVLQGL LRPLFKNTSV
11051 GPLYSGSRLT LLRPEKDGEA TGVDALCTHR PDPTGPGLDR EQLYLELSQL
11101 THSITELGPI TLDRLSLYVN GFTHRSSVPT TSTGVVSEEP FTLNFTINNL
11151 RYMADMGQPG SLKFNITDNV MKHLLSPLFQ RSSLGARYTG CRVIALRSVK
11201 NGAETRVDLL CTYLQPLSGP GLPIKQVFHE LSQQTHGITR LGPYSLDKDS
11251 LYLNGYNEPG LDEPPTTPKP ATTFLPPLSE ATTAMGYHLK TLTNFTISN
11301 LQYSPDMGKG SATFNSTEGV LQHLLRPLFQ KSSMGPFYLG CQLISLRPEK
11351 DGAATGVDTT CTYHPDPVGP GLDIQQLYWE LSQTHGVGTQ LGFYVLDKDS
11401 LFINGYAPQN LSIRGEYQIN PHIVNWNLSN PDPTSSEY

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11451 TLYKGSQ LHD TFRFCLVTNL TMDSVLTVK ALFSSNLDPS LVEQVFLDKT
11501 LNASFHWLGS TYQLVDIHVT EMESVYQPT SSSSTQHFYL NFTITNLPYS
11551 QDKAQPGTTN YQRNKRNIED ALNQLFRNSS IKSYFSDCQV STFRSVPNRH
11601 HTGVDSL CNF SPLARRVDRV AIYEEFLRMT RGTQLQNFT LDRSSVLVDG
11651 YSPNRNEPLT GNSDLFFWAV ILIGLAGLLG LITCLICGVL VTTRRRKKEG
11701 EYNVQQQCPG YYQSHLDLED LQ

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TABLE 22

CA125 Repeat Nucleotide Sequence
(SEQ ID NO: 307)

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1 ACTGCTGGCC CTCTCCTGGT GCCATTACCC CTCAACTTCA CCATCACCAA
10 51 CCTGCAGTAT GAGGAGGACA TGCATCGCCC TGGATCTAGG AAGTTCAACA
101 CCACAGAGAG GGTCTGCAG GGTCTGCTTA GTCCCATATT CAAGAACACC
151 AGTGTGGGCC CTCTGTACTC TGGCTGCAGA CTGACCTCTC TCAGGTCTGA
15 201 GAAGGATGGA GCAGCCACTG GAGTGGATGC CATCTGCATC CATCATCTTG
201 ACCCCAAAAG CCCTGGACTC AACAGAGAGC GGCTGTACTG GGAGCTGAGC
20 301 CGACTGACCA ATGGCATCAA AGAGCTGGGC CCCTACACCC TGGACAGGAA
351 CAGTCTCTAT GTCAATGGTT TCACCCATCG GACCTCTGTG CCCACCACCA
401 GCACTCCTGG GACCTCCACA GTGGACCTTG GAACCTCAGG GACTCCATTC
25 451 TCCCTCCCAA GCCCCGCA

TABLE 23

CA125 Repeat Amino Acid Sequence
(SEQ ID NO: 308)

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35 1 TAGPLLVPFT LNFTITNLQY EEDMHRPGSR KFNTTTERVLQ GLLSPIFKNT
51 SVGPLYSGCR LTSLRSEKDG AATGVDAICI HHLDPKSPGL NRERLYWELS
101 RLNGIKELG PYTLDRNSLY VNGFTHRTSV PTTSTPGTST VDLGTSGTPF
40 151 SLPSPA